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Population Variation in Biomonitoring Data for Persistent Organic Pollutants (POPs): An Examination of Multiple Population-Based Datasets for Application to Australian Pooled Biomonitoring Data

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Abstract

Background. Australian national biomonitoring for persistent organic pollutants (POPs) relies upon age-specific pooled serum samples to characterize central tendencies of concentrations but does not provide estimates of upper bound concentrations. This analysis compares population variation from biomonitoring datasets from the US, Canada, Germany, Spain, and Belgium to identify and test patterns potentially useful for estimating population upper bound reference values for the Australian population.

Methods. Arithmetic means and the ratio of the 95th percentile to the arithmetic mean (P95:mean) were assessed by survey for defined age subgroups for three polychlorinated biphenyls (PCBs 138, 153, and 180), hexachlorobenzene (HCB), p,p-dichlorodiphenyldichloroethylene (DDE), 2,2',4,4' tetrabrominated diphenylether (PBDE 47), perfluorooctanoic acid (PFOA) and perfluoroctane sulfonate (PFOS).

Results. Arithmetic mean concentrations of each analyte varied widely across surveys and age groups. However, P95:mean ratios differed to a limited extent, with no systematic variation across ages. The average P95:mean ratios were 2.2 for the three PCBs and HCB; 3.0 for DDE; 2.0 and 2.3 for PFOA and PFOS, respectively. The P95:mean ratio for PBDE 47 was more variable among age groups, ranging from 2.7 to 4.8. The average P95:mean ratios accurately estimated age group-specific P95s in the Flemish Environmental Health Survey II and were used to estimate the P95s for the Australian population by age group from the pooled biomonitoring data.

Conclusions. Similar population variation patterns for POPs were observed across multiple surveys, even when absolute concentrations differed widely. These

patterns can be used to estimate population upper bounds when only pooled sampling data are available.

1 Introduction

National biomonitoring efforts designed to characterize the levels and distribution of environmental chemical pollutants in populations have typically relied upon a sampling and analysis strategy including hundreds or thousands of individual biological samples. Such efforts are underway in countries including the United States (the National Health and Nutrition Examination Survey, or NHANES), Canada (the Canadian Health Measures Survey, or CHMS), Germany (the German Environmental Survey, GerES), and others (Porta et al. 2008; Schoeters et al. 2011). Biomonitoring programs are resource intensive, often requiring an extensive infrastructure and expertise dedicated to population sampling and significant financial resources to analyze the collected samples (Porta et al. 2009; Porta 2012). Such detailed sampling strategies allow cross-sectional analyses for potential associations with both environmental sources of contamination and with health outcomes. However, if the goal of the effort is to characterize population exposure levels and document spatial and temporal trends, other approaches may be considered.

In Australia and elsewhere, a series of studies relying on multiple pooled serum samples, a less resource-intensive approach, has been employed (Karrman et al. 2006; Toms et al. 2009a; Toms et al. 2009b). Reliance on analysis of multiple pooled samples allows characterization of central tendencies of concentrations in the age, gender, and geographical groups sampled. This approach has produced information allowing evaluation of patterns with age, gender, region of Australia, and, over time, information about temporal trends in the central tendency of measured chemical concentrations. Analytes examined to date include dioxin-like compounds, polychlorinated biphenyls

(PCBs), organochlorine pesticides (OCPs), polybrominated diphenylethers (PBDEs), and perfluorinated compounds (PFCs).

While the pooling approach allows estimation of central tendencies (specifically, arithmetic means, under the condition of equally weighted samples contributing to each pool) of concentrations in the sampled subgroups, it does not provide direct information about population variation in biomarker concentrations. Characterization of population variation –and in particular, estimation of typical upper bound concentrations–may provide benchmarks for assessing whether individuals have biomarker concentrations beyond those typically observed in the population. For example, the German Human Biomonitoring Commission estimates reference values at the 95th percentile (RV_{95}), for use in identifying individuals with unusual exposure levels (Angerer et al. 2011). Characterization of population upper bounds for toxic compounds also allows comparison with health-based screening values, when available, to assess whether general population levels approach or exceed such guidance values.

Statistical approaches have been published to estimate population variation based on variation in concentrations measured in multiple pools from a given population or subpopulation (Caudill et al. 2007; Caudill 2010, 2011, 2012). These approaches rely upon parametric assumptions regarding the shape of the underlying population distribution. As an alternative, this analysis examines empirical patterns in survey data based on the hypothesis that biological variability in processes relative to the accumulation and elimination of such compounds may be similar across populations, leading to similar

degrees of variation in biomarker concentrations in different populations, even when the absolute levels of exposure differ. Specifically, variations in biomarker concentrations of persistent compounds within a population and age group that are exposed to a given matrix of environmental concentrations usually are controlled by a few factors. These include interindividual variation in metabolism and elimination rates, interindividual variation in long-term exposure rates (for example, high fat vs. low fat diet, for lipophilic compounds), history of breast feeding, and, in the case of lipophilic compounds, interindividual variation in lipid content of blood (Bernert et al. 2007; Phillips et al. 1989; Porta et al. 2009). The net effect of these factors on the degree of variation of biomarker concentrations may be similar across different populations, even if absolute exposure levels are not.

This project examined available biomonitoring datasets from the US National Health and Nutrition Examination Survey (NHANES), the Canadian Health Measures Survey (CHMS), the German Environmental Survey (GerES), the Catalan Health Interview Survey (CHIS), and the Flemish Environmental Health Survey II (FLEHS II) to inform interpretation of the Australian pooled biomonitoring data. The objectives of the present study were to:

- Compare population subgroup arithmetic mean concentrations of the subject analytes in Australian pools to those observed in datasets from the US, Canada, Germany, and Catalonia; and
- Assess variation within population subgroups across available datasets for similarity and differences for key persistent organic pollutants (POPs).

We use the results of this analysis to estimate population 95th percentiles (with confidence limits) for the Australian age groups based on the pooled sample means and discuss the estimated levels in the context of health risk screening values, where available.

2 Methods

2.1 Target analytes

The focus of this analysis is on persistent chemicals that are found widely in the general populations in countries around the world. Specifically, we included analytes that are likely to be detected at high rates (so that methods for imputation of non-detected concentrations would not be influential in the calculation of mean or upper percentile statistics) and that have been studied in multiple population-representative studies. For this effort we selected three indicator polychlorinated biphenyls (PCBs), 2,2',3,4,4',5'-hexachlorobiphenyl (PCB 138), 2,2',4,4',5,5'-hexachlorobiphenyl (PCB 153), and 2,2',3,4,4',5,5'-heptachlorobiphenyl (PCB 180); the organochlorine pesticides (OCPs) hexachlorobenzene (HCB) and p,p'-dichlorodiphenyldichloroethylene (DDE); two perfluorinated compounds, perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA); and one brominated diphenyl ether, 2,2',4,4'-tetrabromodiphenyl ether (PBDE 47). Not all of these analytes were available in all datasets.

166 *2.2 Datasets*

167 Pooled sample biomonitoring data for the Australian population from three cycles
168 were included for comparison to the mean values for each analyte from the other
169 surveys in order to assess whether the Australian mean pool concentrations are
170 similar to, or different from, those observed in other countries. The Australian
171 pooled sampling campaigns rely upon surplus sera obtained from anonymized
172 samples collected from community pathology laboratories for selected demographic
173 (age and sex) strata. The samples are not selected based on a stratified or census-
174 based statistical sampling strategy, but rather are convenience samples collected
175 during the designated time periods. Results from the 2002-2003, 2008-2009, and
176 2011-2012 sampling efforts were included. For each cycle and analyte, four pools
177 composed of 100 individual serum samples were analyzed for each age group. For
178 the current analysis, the average and inter-pool standard deviation (SD) of the
179 analyte concentration in multiple age-stratified pools (combined sexes) were
180 calculated. The 95 percent confidence limits on the average concentrations for each
181 age strata were calculated as the mean+/- 1.96*SD, which represent the 2.5^{th} and
182 97.5^{th} percentiles of the normal distribution represented by the observed mean and
183 SD.
184
185 Biomonitoring data for the target analytes were obtained from statistically
186 representative population survey datasets from five countries: Germany, the United
187 States, Canada, the Catalonian region of Spain, and the Flemish region of Belgium.
188 Each of the datasets is described in more detail below.

The German Environmental Survey (GerES) III is a probability sample selected in 1998 to be representative for the German population with regard to region (East-/West-Germany), community size, age (18 to 69 years) and gender (Kolossa-Gehring et al. 2012a; Kolossa-Gehring et al. 2012b; Schulz et al. 2007). GerES IV was conducted in 2003-2006 and focused on children ages 7 to 14 who were participants of the National Health Interview and Examination Survey on Children and Adolescents (Schulz et al. 2012). The GerES datasets provided data on the three indicator PCBs, HCB, and DDE. The GerEs data are presented in terms of concentrations in whole blood, while data from the other surveys included in this evaluation present data on the basis of wet weight concentrations in serum or plasma as well as lipid-adjusted serum or plasma concentrations. As a result, the arithmetic means of the concentrations measured in the GerES cycles cannot be compared directly to the other surveys.

The US National Health and Nutrition Examination Survey (NHANES) is a stratified multistage probability sample of the civilian non-institutionalized population of the U.S., and is conducted on a continuous basis with datasets reported for two year periods. For the present analysis, we used the 2003-2004 cycle data, which reports the most recent data available for PCBs, HCB, pp-DDE, and PBDE 47. For PFOA and PFOS, data have been reported each two-year cycle from 1999 through 2010. For this analysis, the oldest and the most recent available datasets were selected in order to obtain the two datasets on PFOA and PFOS in the US that are most

separated in time. The rationale for this selection is that we are interested in independent evaluations of population variation including evaluations at different absolute concentration levels. While the NHANES surveys conducted at different time periods cannot be considered independent of one another because the population shares the same historical pattern of exposures up until the time of the first survey, the separation in time at least increases somewhat the independence of the observations as well as providing datasets with different absolute concentrations.

The Canadian Health Measures Survey (CHMS) targets the Canadian population aged 6 to 79 years living at home and residing in the ten provinces and three territories of Canada, estimated to represent approximately 96.3% of the Canadian population (Statistics Canada 2011). The cycle 1 data used in the current analysis were collected from 2007 to 2009. Data for all of the target analytes were available in the CHMS cycle 1 dataset.

The Catalan Health Interview Survey (CHIS) was conducted in 2002 and is a representative sample of the non-institutionalized population in Catalonia (Spain), which had a population of 6,506,440 inhabitants in 2002 (Porta et al. 2010). The CHIS used a multiple-stage random sampling strategy and it provides data on the three target PCBs, HCB, and DDE for this analysis.

The Flemish Environment and Health Survey II (FLEHS II) examined the concentrations of numerous analytes in newborns, their mothers, and in adolescents (Schoeters et al. 2011; Schroijen et al. 2008; Staessen et al. 2001). Concentrations of all of the target analytes for this evaluation were measured in representative samples of cord blood plasma in newborns and women of reproductive age (through age 45) in 2008-2009 and in adolescents from 2008-2011. Concentrations of PFOA and PFOS were also measured in young adults through age 40 in 2008-2011 (Schoeters et al. 2011).

2.3 Statistical analysis

The primary goal of this analysis was to provide information that could be used to estimate a 95th percentile for Australian population subgroups by age based on the pooled sampling effort conducted periodically in Australia. For the Australian pooled analyses, pools are assembled for six age groups: 0 to 4, 5 to 15, 16 to 30, 31 to 45, 46 to 60, and >=61 years. Thus, for these analyses, each of the included datasets was stratified into corresponding age groups.

Bootstrapping procedures. The analysis focused on the estimation of the arithmetic mean and the ratio of the 95th percentile to the arithmetic mean (P95:mean ratio), as well as confidence intervals for these estimates, for each age group from the US, Canadian, German, and Catalan datasets. The estimation of confidence intervals was accomplished using bootstrapping approaches. For each dataset and age stratum a two-step process was followed. First, the "true" arithmetic mean and P95:mean

ratio were calculated using the appropriate dataset-specific survey sample weights. Then that age stratum was resampled with replacement 1,000 times. For each iteration, the arithmetic mean and the P95:mean ratio were calculated using the appropriate weights and recorded. The 2.5^{th} and 97.5^{th} percentiles of the resulting 1,000 estimates for the mean and P95:mean ratio were then selected as the 95% confidence intervals on the point estimates of the "true" mean and P95:mean ratios. All analyses were conducted using Stata 12.1, except for those on the CHMS dataset, which was analyzed by scientists at Statistics Canada using SAS 9.2 and SUDAAN 10.0.1 as a SAS-callable extension. In addition, the analysis of the CHMS dataset analyses relied upon the previously-established bootstrap replicate weights for that dataset, which provide 500 rather than 1,000 iterations of the calculation.

Arithmetic means for each analyte and age group were compared across populations. The observed P95:mean ratios were examined for patterns across surveys and across age groups through visual inspection, including consideration of the width and overlap of confidence intervals.

Unified ratios and validation. Four survey datasets (NHANES, GerES, CHMS, and CHIS) were available for the three PCB compounds as well as HCB and DDE. Of these, the bootstrapped iterations of P95:mean ratios were available for all except the CHMS. Using the bootstrapped iterations from the three other surveys, we constructed a "unified" estimate of the P95:mean ratios with confidence intervals for each age group and over all age groups for each of these compounds. The

bootstrapped iterations of the P95:mean ratio for each analyte, age group, and survey (except for the CHMS dataset, for which the estimates were not available, and the FLEHS II survey, which was used as the validation set; see below) were appended. One thousand bootstrapped iterations were available for each included survey. These bootstrapped iterations were combined for each age groups, resulting in 3,000 bootstrap iterations of the ratio per age group (the surveys were weighted equally). The median and 2.5th and 97.5th percentiles of the combined iterations of the P95:mean ratios for each analyte and age group were calculated and reported as a unified estimate with 95% CI from across the US, German, and Catalan surveys. Because of the lack of apparent systematic variation in the P95:mean ratios with age, we further combined the iterations across all three surveys and age groups for each of the five analytes (PCBs, HCB and DDE). The resulting 14,000 iterations were used to generate an "all ages" median P95:mean ratio with 95% confidence intervals across all age groups and the three surveys (each age group and survey weighted equally).

The FLEHS II data were used as a validation dataset. The "true" arithmetic mean and 95th percentile from the FLEHS II survey for each analyte was calculated for each included age group. Using the unified P95:mean ratio estimates, a "predicted" population 95th percentile (with 95% CI) was estimated by multiplying the true mean for each age group and analyte by the unified ratio (for the five analytes with a calculated unified ratio) or by the ratio from the most recent NHANES dataset and age group when only one or two survey sets were available. Specifically, none of the

303 population-representative datasets allowed estimation of ratios for ages 0 to 4, so
304 ratios obtained for the 5-15 yr age group were applied to the mean concentrations
305 calculated for cord blood data from the FLEHS II dataset to estimate the
306 corresponding 95th percentiles. Similarly, no unified ratio estimate was available for
307 PBDE 47, PFOA, or PFOS, so the ratios from the most recent NHANES survey data
308 (2003-2004 for PBDE 47 and 2009-2010 for the PFCs) were used for those analytes.
309 The predicted 95th percentile and confidence intervals for each age group and
310 analyte was compared to the true 95th percentile to evaluate if the distributions
311 observed in the other datasets could accurately predict the upper end of the
312 observed distribution in the FLEHS II dataset based on the arithmetic mean
313 measures in that dataset.
314
315 *2.4 Prediction of 95th percentiles for the Australian population and comparison to*
316 *health risk-based benchmarks*
317 The same ratios evaluated in the validation exercise against the FLEHS II dataset
318 were applied to the Australian pooled sampling results for 2011-2012 to estimate
319 population age group-specific 95th percentiles. The resulting 95th percentiles were
320 compared to an available screening criterion for PCBs (ANSES 2010) and
321 Biomonitoring Equivalents for HCB and DDE (Aylward et al. 2010; Kirman et al.
322 2011, respectively) to provide a perspective on the potential population health
323 implications of the estimated upper bound reference levels in the Australian
324 population. To our knowledge, no health risk screening values based on biomarker
325 concentrations are available for the remaining analytes in the analysis.

3 Results

Each of the datasets included in this analysis covered somewhat different age ranges and numbers of sampled participants (Table 1). Because the purpose of the analysis is to inform the interpretation of the Australian pooled biomonitoring surveys, age groups were defined using the same cutpoints used by the Australian sampling program. Data representing the youngest age group (0 to 4 years) was not available for these analytes from any of the available datasets, although arguably the cord blood data collected in the FLEHS II may be most relevant. The coverage of the 5-to-15 age group was only partial, with substantial overlap in the GerES IV dataset (ages 7 to 14 included) and partial overlap in the NHANES datasets (12 to 15). Similarly, the cutoff ages at the upper end varied by dataset.

3.1 Comparison of arithmetic means and P95:mean ratios across surveys

The arithmetic means and 95% CI and the P95:mean ratios and 95% CIs for each analyte and age group across surveys are presented graphically in Figures 1 through 3. These statistics are also tabulated in the Supplementary Data. The results from the comparison of datasets are discussed below on a compound-by-compound basis. For each compound several issues are discussed. The plots of arithmetic mean concentrations for each compound allow comparison of the mean concentrations from the Australian pooled sampling to the arithmetic mean concentrations from the other surveys and examination of the trends in the Australian pooled sampling over the three sampling time frames included. The plots of the P95:mean ratios by

age group for each compound allow examination of potential trends in this metric with age with each survey as well as evaluation of the consistency of results among surveys. Tables of population statistics for each survey are available in Supplementary Data.

PCBs 138, 153, and 180. Arithmetic mean concentrations of each of the PCB compounds examined displayed a marked pattern of increasing concentrations with age in every survey, consistent with previous studies (see, for example, Patterson et al. 2009; Figure 1). The only exception to this pattern was for the two youngest age groups as examined by the Australian pooling studies. In the two most recent cycles of Australian studies (2008-9 and 2011-12), average pooled sample concentrations from the youngest age group, 0 to 4 years, were as high as or higher than the concentrations in the next oldest age group, 5 to 15 years. No data for the youngest age group were available from any of the other surveys, so this result likely represents a previously unexamined pattern that may relate to elevated exposure via lactation followed by growth dilution (Verner et al. 2009; Verner et al. 2013).

Arithmetic mean concentrations varied substantially among surveys for each age group examined. In general, the CHIS dataset had the highest arithmetic mean concentrations, with concentrations in each age group for each of the PCB analytes more than ten times higher than the concentrations in the most recent two Australian pooled sampling efforts, which were generally the lowest levels observed in each age group. The CHIS was conducted at the earliest time point of any of the

included surveys that present data on a lipid-adjusted basis, and at least some of the difference in arithmetic means between this survey and the current Australian pooled data is due to the likely decrease in levels over time in the environment and in the population since the CHIS was conducted. The US and Canadian datasets generally exhibited similar arithmetic mean concentrations at each age group, with the means intermediate between the Australian and CHIS mean concentrations.

In contrast to the results for the arithmetic means, the P95:mean ratios observed for each PCB compound were relatively similar, both across age groups and among the different surveys. P95:mean ratios for all three compounds were generally between 2 and 2.5, without any clear or consistent patterns of difference by age or survey. The only exception was for PCB 180 for the age group 5 to 15 years. Data from the GerES IV and NHANES survey both suggest that the P95:mean ratio is approximately 3 for this analyte in this age group, somewhat higher than observed in the older age groups.

HCB and DDE. The arithmetic mean concentrations for HCB and DDE also displayed a trend of increasing concentrations with increasing age in each of the datasets included (Figure 2). As with the PCB compounds, the most recent Australian pooled sample analyses tended to show the lowest concentrations, with a trend of decreasing concentrations with each subsequent survey. As with the PCBs, the Catalan data had the highest mean concentrations, particularly for HCB concentrations, which were often 10-fold or more higher than observed in the other

surveys at each age group. In contrast, DDE mean concentrations were somewhat higher in the Catalan data compared to the other surveys (Porta et al. 2010; Porta et al. 2012).

The P95:mean ratios from the different surveys were not as consistent for HCB as for the PCB compounds, varying both within and between age groups among the different surveys over a range from about 1.5 to 2.5. In particular, the NHANES dataset had lower ratios for each of the adult age groups compared to the other surveys, although the ratio for the 5-15 age group was similar to that observed in the GerES IV dataset. For DDE, the P95:mean ratios were also somewhat less consistent, without a clear pattern either across age groups or surveys. Overall, the DDE ratios were higher than those observed for the other analytes, ranging from approximately 2 to 3.5.

PBDE 47. Data for PBDE 47 was available only from the Australian pooled sample analyses, the US NHANES survey, and the CHMS (Figure 2). The arithmetic mean concentrations of PBDE were lowest in the most recent Australian pooled analyses, and highest in the US NHANES survey. In general, the most recent (2011-2012) Australian pooled data means for each age group were approximately 10-fold lower than the corresponding values from the 2003-2004 US NHANES survey. Unlike for the PCB and organochlorine pesticide compounds, there was little evidence of an increasing trend in average concentration with increasing age in any of the surveys. This may be a consequence of several factors, including a less-distinct or absent

418 temporal trend of declining exposures over time and more active metabolism of this
419 compound, resulting in somewhat shorter half-life of elimination (Quinn and Wania,
420 2012).
421
422 P95:mean ratios were available only from the NHANES and CHMS surveys and did
423 not present a consistent pattern, either within or between age groups. Ratios
424 ranged from approximately 2.7 to nearly 5. Both of these datasets represent North
425 American populations, where exposure to brominated flame retardants has been
426 substantially higher than in European and other populations (Harrad et al. 2010;
427 Roosens et al. 2009). As noted above, PBDE 47 is actively metabolized, and thus
428 variations in individual efficiency of metabolism may vary somewhat more than for
429 the more passive elimination mechanisms that dominate for the chlorinated
430 compounds discussed above. In addition, indoor dust may be a more important
431 exposure pathway for brominated flame retardants compared to PCBs and OCPs,
432 potentially resulting in more variable exposure levels within populations.
433
434 *PFOS and PFOA.* Arithmetic mean concentrations for PFOS and PFOA (Figure 3)
435 from the 2008-2009 Australian pooled sampling, the CHMS 2007-2009 data, and the
436 2009-2010 NHANES data are fairly similar to one another and lower than the
437 concentrations observed in the earlier Australian sampling (2002-2003) and the
438 earlier NHANES survey (1999-2000). For PFOA, the CHMS survey appears to have
439 the lowest mean concentrations for each age group and no clear differences were
440 observed among age groups. For PFOS the concentrations are very similar among

all of the more recent datasets, again, with no striking trend by age group. P95:mean ratios are quite similar among all age groups for PFOA, ranging between approximately 1.7 and 2.2. For PFOS, there is somewhat more variation, but overall, the ratios again range fairly narrowly, from about 1.7 to 2.6.

3.2 Unified Ratios

The availability of multiple datasets for the three PCB compounds, HCB, and DDE, presented the opportunity to combine the bootstrapped estimates of P95:mean ratios from all of the datasets both within and across age groups. As discussed in methods, confidence intervals on the ratios were estimated based on 1,000 bootstrapped estimates of the P95:mean ratio for each age group and compound for the US NHANES, the GerES III and GerES IV surveys, and the CHIS. Bootstrapped ratios were also calculated by the CHMS program, but the individual iterated bootstrapped values were not available for combination with the other surveys. As a result, 1000 bootstrapped estimates for each age group were combined from the US, German, and Catalan survey analyses in order to estimate unified age-specific and overall ratios for the PCBs, HCB, and DDE (Table 2).

Only two datasets were available for examination for patterns in PBDE 47 P95:mean ratios, those from CHMS and NHANES (Figure 2). As discussed above, the CHMS bootstrapped iterations were not available, and the pattern of results was quite variable both between surveys and across age groups. As a result, no "unified" estimate of ratios was attempted for PBDE 47. Furthermore, given the substantial

464 inconsistencies in results across surveys and across and within age groups, it is
465 difficult to identify any specific dataset that would be most appropriate to
466 recommend for use as a model for the P95:mean ratio for estimating the 95th
467 percentile in the Australian population data based on the pooled results for this
468 compound. In the absence of a more consistent set of ratios, the age group-specific
469 US NHANES P95:mean ratios for PBDE 47 were applied to estimate 95th percentile
470 concentrations in the FLEHS II survey (as a validation exercise) and for the
471 Australian population based on their pooled sample data.
472
473 Three datasets were examined for PFOS and PFOA. As discussed above, the CHMS
474 bootstrapped iterations were not available for inclusion in a unified analysis.
475 However, because the observed P95:mean ratios across the two NHANES surveys (a
476 decade apart) and the CHMS survey were quite consistent both within and between
477 age groups, the results from the most recent NHANES survey are proposed as
478 providing a reasonable estimate of the P95:mean ratio for use with these
479 compounds. These are presented in Table 3.
480
481 *3.3 Validation*
482 The FLEHS II data were used as a validation dataset. The calculated arithmetic
483 means and 95th percentiles for each age group and analyte are presented in Figure 4
484 along with the predicted 95th percentiles obtained by applying the all-ages unified
485 P95:mean ratios estimated from the analyses described above for the PCBs, HCB,
486 and DDE. Unified ratios were not available for PFOA, PFOS, and PBDE 47, so age-

specific ratios from the most recent available NHANES dataset were applied for those analytes. Because no ratios for the youngest age group were available for these analytes, the NHANES ratios for the next oldest group were used to predict the 95th percentiles in cord blood samples. Table 3 summarizes the applied ratios used in the estimation of 95th percentiles from the FLEHS II dataset.

The predicted 95th percentiles generally matched well with observed ratios in the FLEHS II dataset for all ages and analytes, with some exceptions (Figure 4). P95 concentrations for the 16 to 30 year age groups tended to be underestimated for the PCBs, DDE, and PBDE 47. However, given the wide confidence intervals on the point estimates from the FLEHS II resulting from the relatively small number of observations in this age group in the dataset, the estimates are acceptable. These results suggest that application of these ratios to the Australian pooled sample concentrations to estimate Australian 95th percentile concentrations may provide useful estimates.

Of particular interest in this analysis is the fact that cord blood plasma concentration distributions in the FLEHS II were well estimated by the available ratios for all age groups (or for older children, in the case of PFOA and PFOS). This is perhaps not surprising, since the concentrations in cord blood are likely to be influenced by and proportional to maternal concentrations through both in utero and lactational transfer. Such exposure routes do suggest caution in application of this approach if factors such as duration of breast-feeding are substantially different

between populations. However, the results here do support the idea that, at least in some circumstances, cord blood sampling and analysis for the purposes of population characterization could be conducted using pooled samples without loss of too much information, thus maximizing the utility of the limited sample volumes available.

3.4 Prediction of Australian Population Upper Bound Reference Values and Comparison to Health- or Risk-Based Screening Values

The same unified or selected P95:mean ratios evaluated in the validation exercise (Table 3) were applied to the Australian 2011-2012 pooled means to estimate the current 95th percentiles in the sampled Australian age groups. The resulting analyte- and age group-specific P95 estimates are presented in Table 4. The confidence intervals on the estimates should be noted and considered when interpreting and applying the 95th percentile estimates. And, as noted above, estimates for PBDE 47 should be considered especially carefully, given the potential for varying exposure pathways across different populations (Harrad et al. 2010; Roosens et al. 2009).

Available non-cancer health risk screening criteria are summarized in Table 5. The values for HCB and DDE are Biomonitoring Equivalents (BE), estimates of the steady-state biomarker concentrations corresponding to the cited exposure guidance values (Hays et al. 2008). The value for PCBs was derived by the French Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du

travail (ANSES) based on studies relating human health outcomes to serum lipid PCB concentrations (Agence nationale de securite sanitaire Alimentation Environnement Travail (ANSES) 2010). No health risk-based screening values based on biomarker concentrations were found for the other chemicals in this analysis.

HCB. For HCB, the BE value cited here is 47 ng HCB/g lipid, which is the estimated steady-state serum lipid concentration corresponding to the Minimal Risk Level (MRL) from the US Agency for Toxic Substances and Disease Registry (ATSDR) (5E-05 mg/kg-d). This value was derived by application of an uncertainty factor of 300 to a lowest-observed-adverse-effect-level (LOAEL) for mild hepatic toxicity in a multi-generation rat study. Other BE values are available; however, this is the most stringent available non-cancer value (Aylward et al. 2010). Because of the application of uncertainty factors, exceedence of the BE value of 47 ng/g serum lipid would not necessarily be expected to result in adverse effects in humans. However, the value serves as a conservative screening value to protect against potential HCB toxicity. The Australian average pool concentrations are below this value for all age groups. The P95 estimates for all age groups are below this level except for the oldest age group (>60 years). The estimated P95 for this age group is 83 ng/g lipid, or nearly double the BE value, suggesting a potential concern.

BE values based on cancer risk from HCB (derived from rat bioassay data) are also available. The Australian mean and P95 values across all age groups are in the

range of 5 to 83 ng/g lipid. These levels are consistent with BE values corresponding to cancer risk estimates in the range of 1 in 1 million to 1 in 100,000 (Aylward et al. 2010). This range of cancer risk is generally considered by the USEPA to be in the target range for acceptable risks.

DDE. BE values for summed DDT and metabolites DDE and DDD in serum lipid are available (Kirman et al. 2011). Generally DDE is the predominant contributor to this sum. For noncancer endpoints, the BE value corresponding to the USEPA reference dose (RfD, which is also derived based on rat hepatic toxicity data) is 5,000 ng/g lipid. The Australian pool means range from 83 to 665 ng/g lipid, and P95 estimates range from 245 to approximately 2,000 ng/g lipid, and so are below the non-cancer BE value. Based on estimates of cancer risk derived from rat bioassay data, the highest Australian P95 (for age group >60 yrs) corresponds to an estimated cancer risk of 5 in 100,000, while the lowest pool mean value corresponds to an estimated cancer risk level of 2.5 in 1 million.

PCBs. The French ANSES guidance values are based on human health studies that examined associations between human health outcomes and PCB serum lipid concentrations (ANSES 2010). The ANSES evaluation concluded that the most sensitive responses appeared to be altered neurodevelopmental endpoints in children exposed in utero and via lactation, and a "concentration of concern" of 700 ng/g lipid was set for infants, children, and women of reproductive age. The evaluation also concluded that for other adults outside these categories, a value of

1,800 ng/g lipid would be protective. These values are calculated as the sum of PCB 138, 153, and 180 times a factor of 1.7.

In the Australian pooled data, we do not have a direct assessment of the sum of PCBs 138, 153, or 180 at the P95. However, a conservative approach would be to sum the P95 estimates for the three congeners and multiply this sum by 1.7. When calculated this way, none of the Australian age groups approach the ANSES concentrations of concern, suggesting relatively little concern based on the current health risk assessments for PCBs.

4 Discussion

The results from this analysis suggest that, for many of the persistent chemicals examined here, the degree of variation between typical upper bound concentrations as estimated by the 95th percentile in the population and the arithmetic mean in the population is reasonably similar between populations, even when the absolute levels of the analyte vary substantially across these populations. This observation is consistent with the hypothesis that population variation in biomarker concentrations for these persistent analytes may be heavily influenced by factors that are generally similar regardless of the absolute level of exposure, for example, distribution of patterns of dietary fat intake and distribution of interindividual variation in intrinsic metabolic or elimination efficiency for these compounds.

The general similarity in the observed P95:mean ratios across surveys suggests that the distribution of concentrations of each of these analytes in all of these populations (within an age group) can be reasonably estimated as a lognormal distribution with different geometric mean values, but similar geometric standard deviations. In a lognormal distribution, the log of the arithmetic mean (AM) is a function of the geometric mean (GM) and geometric standard deviation (GSD) (Caudill et al. 2007):

$$\log AM = \log GM + \frac{(\log GSD)^2}{2} \quad (1)$$

And the log of the 95th percentile (P95) is:

$$\log P95 = \log GM + 1.64 * \log GSD \quad (2)$$

The P95:mean ratio would then be the difference of equation 2 and equation 1:

$$\log\left(\frac{P95}{AM}\right) = \log GM + 1.64 * \log GSD - \left(\log GM + \frac{(\log GSD)^2}{2}\right) \quad (3)$$

which is

$$\log\left(\frac{P95}{AM}\right) = 1.64 * \log GSD - \frac{(\log GSD)^2}{2} \quad (4)$$

622 Thus, the P95:mean ratio in the theoretical case of a lognormal distribution is
623 independent of the geometric mean and depends only on the geometric standard
624 deviation of the distribution.
625
626 This analysis provides for the first time an integrated picture of the patterns of
627 arithmetic mean and population variation in selected POPs concentrations across
628 several national biomonitoring surveys. The inclusion of data from several
629 geographic areas and over a number of time periods from surveys including
630 thousands of individual samples is a significant strength of the analysis. However,
631 there are also numerous cautions and limitations associated with this analysis. It is
632 an empirical evaluation of the patterns observed for specific analytes, populations,
633 and age groups, and, as such, is somewhat limited in its generalizability to other
634 analytes. In particular, no data were available from the various population
635 representative surveys for the youngest age group (ages less than 1 to 4), and the
636 coverage of the next oldest age group (5 to 15) was only partial in the various
637 datasets. The dataset used for validation (FLEHS II) did not assess levels in the
638 oldest two age groups, although the consistency among the included datasets is, in
639 itself, a degree of validation. Finally, we did not break out the analysis of variation
640 by sex. Since PFOA and PFOS do show trends by sex, with adult males often showing
641 higher levels than adult females (Kato et al. 2011), a sex-specific analysis could be of
642 interest for these compounds in particular.
643

644 This approach, of applying empirically observed degrees of variation to estimated
645 population arithmetic means, might cautiously be applied to additional analytes
646 beyond those evaluated here based on examination of the P95:mean ratios from the
647 NHANES dataset, which is one of the largest available ongoing programs,
648 particularly if factors relevant to population variation in exposures are partly
649 understood. However, the application of the approach might be most appropriate
650 for relatively persistent analytes for which the distribution of concentrations in the
651 population is not strongly influenced by within-day, within-individual variation
652 (Aylward et al. 2012; Pleil and Sobus 2013), and for analytes that exhibit generally
653 lognormal distributions in the NHANES dataset.
654
655 The estimates of 95th percentiles for the Australian population made using this
656 approach based on the pooled sampling efforts conducted to date have several
657 applications. Individual biomonitoring results (for example, for workers with
658 potential exposure to these compounds) can be assessed to identify subjects with
659 levels above those expected in the general population. Thus, when needed for
660 evaluation of individual biomonitoring data, these values can be used as provisional
661 estimates of the upper end of a population "reference range" (Angerer et al. 2011),
662 bearing in mind the uncertainties associated with the method and the confidence
663 intervals associated with those estimates, until such time as more comprehensive
664 population-representative datasets can be derived.
665

666 On a population basis, these upper bound levels can be compared to biomarker-
667 based health risk screening values in order to place the estimated range of
668 population biomarker concentrations into a health risk context. For the analytes
669 examined here, screening values include the French ANSES concentration of
670 concern for indicator PCBs (Agence nationale de securite sanitaire Alimentation
671 Environnement Travail (ANSES) 2010) and Biomonitoring Equivalents for
672 DDT/DDE and HCB (Aylward et al. 2010; Aylward et al. 2013; Kirman et al. 2011).
673 The estimated Australian upper bound levels for the various analytes with available
674 screening values were generally below the those screening values, with the
675 exception of HCB in the oldest age group, suggesting that the typical range of
676 concentrations of individual compounds observed in the Australian population
677 (through the 95th percentile) are not likely to result in overt health effects in the
678 Australian population based on current risk assessments.
679
680 The consistency in the degree of variation for a given analyte has implications for
681 attempts to characterize biomarker concentrations in populations that have not
682 previously been studied. The patterns suggest that the population biomarker
683 concentrations of these selected compounds (both the central tendency and a
684 reference upper bound) may be estimated by constructing and analyzing pooled
685 samples from a representative selection of the population, at least as an initial step.
686 Pooled samples provide an estimate of the arithmetic mean concentration in a
687 studied group, although the geometric mean is often regarded as more appropriate
688 measure of central tendency for human biomonitoring data, as it is less influenced

by extreme values. Specific considerations for the design and execution of pooled population biomonitoring studies include decisions on the number of individual samples to be included in pools, the number of replicate pools per population subgroup, and geographical distribution of individual samples comprising the pools (Heffernan et al. 2014). Detailed discussion of these issues is outside the scope of this paper; however, information provided by the variation analyses presented here can assist in some of these decisions. As allocation of resources to biomonitoring programs is considered, the patterns in variation presented here for selected POPs and the empirical approach presented here may prove valuable in obtaining the maximum utility out of data generated under constraints imposed by limited resources or due to limited analytical sensitivity that requires increased sample volumes for quantification of analytes.

5 References

Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES). 2010. Opinion of the French Food Safety Agency on interpreting the health impact of PCB concentration levels in the French population. Available: http://www.anses.fr/Documents/RCCP2008sa0053EN.pdf [Accessed 4 January 2012].

Angerer J, Aylward LL, Hays SM, Heinzow B, Wilhelm M. Human biomonitoring assessment values: approaches and data requirements. Int J Hyg Environ Health 2011; 214:348-60.

Aylward LL, Hays SM, Gagne M, Nong A, Krishnan K. Biomonitoring equivalents for hexachlorobenzene. Regul Toxicol Pharmacol 2010; 58:25-32.

Aylward LL, Kirman CR, Adgate JL, McKenzie LM, Hays SM. Interpreting variability in population biomonitoring data: role of elimination kinetics. J Expo Sci Environ Epidemiol 2012; 22:398-408.

Aylward LL, Kirman CR, Schoeny R, Portier CJ, Hays SM. Evaluation of biomonitoring data from the CDC National Exposure Report in a risk assessment context: perspectives across chemicals. Environ Health Perspect 2013; 121:287-94.

Bernert JT, Turner WE, Patterson DG, Jr., Needham LL. Calculation of serum "total lipid" concentrations for the adjustment of persistent organohalogen toxicant measurements in human samples. Chemosphere 2007; 68:824-31.

724 Caudill SP, Turner WE, Patterson DG, Jr. Geometric mean estimation from pooled
725 samples. Chemosphere 2007; 69:371-80.

726 Caudill SP. Characterizing populations of individuals using pooled samples. J Expo
727 Sci Environ Epidemiol 2010; 20:29-37.

728 Caudill SP. Important issues related to using pooled samples for environmental
729 chemical biomonitoring. Stat Med 2011; 30:515-21.

730 Caudill SP. Use of pooled samples from the National Health and Nutrition
731 Examination Survey. Stat Med 2012; 31:3269-77.

732 Harrad S, de Wit CA, Abdallah MA, Bergh C, Bjorklund JA, Covaci A, et al. Indoor
733 contamination with hexabromocyclododecanes, polybrominated diphenyl ethers,
734 and perfluoroalkyl compounds: an important exposure pathway for people? Environ
735 Sci Technol 2010; 44:3221-31.

736 Hays SM, Aylward LL, LaKind JS, Bartels MJ, Barton HA, Boogaard PJ, et al. Guidelines
737 for the derivation of Biomonitoring Equivalents: report from the Biomonitoring
738 Equivalents Expert Workshop. Regul Toxicol Pharmacol 2008; 51(3 Suppl):S4-15.

739 Karrman A, Mueller JF, van Bavel B, Harden F, Toms LM, Lindstrom G. 2006. Levels
740 of 12 perfluorinated chemicals in pooled australian serum, collected 2002-2003, in
741 relation to age, gender, and region. Environ Sci Technol 2006; 40:3742-48.

742 Kato K, Wong LY, Jia LT, Kuklenyik Z, Calafat AM. Trends in exposure to
743 polyfluoroalkyl chemicals in the U.S. Population: 1999-2008. Environ Sci Technol.
744 2011; 45: 8037-45.

745 Kirman CR, Aylward LL, Hays SM, Krishnan K, Nong A. Biomonitoring equivalents
746 for DDT/DDE. Regul Toxicol Pharmacol 2011; 60:172-80.

747 Kolossa-Gehring M, Becker K, Conrad A, Schroter-Kermani C, Schulz C, Seiwert M.
748 Environmental surveys, specimen bank and health related environmental
749 monitoring in Germany. Int J Hyg Environ Health 2012a; 215:120-6.

750 Kolossa-Gehring M, Becker K, Conrad A, Schröter-Kermani C, Schulz C, Seiwert M.
751 Health-related environmental monitoring in Germany: German Environmental
752 Survey (GerES) and Environmental Specimen Bank (ESB). In: Knudsen L, Merlo F:
753 Biomarkers and Human Biomonitoring Vol. 1: Ongoing Programs and Exposures.
754 RSC Publishing, Cambrigde, UK, 2012b, p. 16-45.

755 Patterson DG, Jr., Wong LY, Turner WE, Caudill SP, Dipietro ES, McClure PC, et al.
756 Levels in the U.S. population of those persistent organic pollutants (2003-2004)
757 included in the Stockholm Convention or in other long range transboundary air
758 pollution agreements. Environ Sci Technol 2009; 43:1211-8.

759 Phillips DL, Pirkle JL, Burse VW, Bernert JT, Jr., Henderson LO, Needham LL.
760 Chlorinated hydrocarbon levels in human serum: effects of fasting and feeding. Arch
761 Environ Contam Toxicol 1989; 18:495-500.

762 Pleil JD, Sobus JR. Estimating lifetime risk from spot biomarker data and intraclass
763 correlation coefficients (ICC). J Toxicol Environ Health A 2013; 76:747-66.

764 Porta M, Puigdomènech E, Ballester F, Selva J, Ribas-Fitó N, Llop S, et al. Monitoring
765 concentrations of persistent organic pollutants in the general population: The
766 international experience. Environ Int 2008; 34:546-61.

767 Porta M, Jariod M, Lopez T, Pumarega J, Puigdomenech E, Marco E, et al. Correcting
768 serum concentrations of organochlorine compounds by lipids: alternatives to the
769 organochlorine/total lipids ratio. Environ Int 2009; 35:1080-5.

770 Porta M, Gasull M, Puigdomenech E, Gari M, Bosch de Basea M, Guillen M, et al.
771 Distribution of blood concentrations of persistent organic pollutants in a
772 representative sample of the population of Catalonia. Environ Int 2010; 36:655-64.

773 Porta M, Pumarega J, Gasull M. Number of persistent organic pollutants detected at
774 high concentrations in a general population. Environ Int 2012; 44:106-11.

775 Quinn CL, Wania F. Understanding differences in the body burden-age relationships
776 of bioaccumulating contaminants based on population cross sections versus
777 individuals. Environ Health Perspect. 2012; 120:554-9.

778 Roosens L, Abdallah MA, Harrad S, Neels H, Covaci A. Exposure to
779 hexabromocyclododecanes (HBCDs) via dust ingestion, but not diet, correlates with
780 concentrations in human serum: preliminary results. Environ Health Perspect 2009;
781 117:1707-12.

782 Schoeters G, Colles A, Den Hond E, Croes K, Vrijens J, Baeyens W, et al. 2011. The
783 Flemish Environment and Health Study (FLEHS) –Second Survey (2007–2011):
784 Establishing Reference Values for Biomarkers of Exposure in the Flemish
785 Population. CHAPTER 2F in Issues in Toxicology No. 9. Biomarkers and Human
786 Biomonitoring, Volume 1: Ongoing Programs and Exposures. L.E. Knudsen and D.F.
787 Merlo. Royal Society of Chemistry, 2011.

788 Schroijen C, Baeyens W, Schoeters G, Den Hond E, Koppen G, Bruckers L, et al.
789 Internal exposure to pollutants measured in blood and urine of Flemish adolescents
790 in function of area of residence. Chemosphere 2008; 71:1317-25.

791 Schulz C, Conrad A, Becker K, Kolossa-Gehring M, Seiwert M, Seifert B. Twenty years
792 of the German Environmental Survey (GerES): human biomonitoring--temporal and
793 spatial (West Germany/East Germany) differences in population exposure. Int J Hyg
794 Environ Health 2007; 210:271-97.

795 Schulz C, Seiwert M, Babisch W, Becker K, Conrad A, Szewzyk R, et al. Overview of
796 the study design, participation and field work of the German Environmental Survey
797 on Children 2003-2006 (GerES IV). Int J Hyg Environ Health 2012; 215:435-48.

798 Staessen JA, Nawrot T, Hond ED, Thijs L, Fagard R, Hoppenbrouwers K, et al. Renal
799 function, cytogenetic measurements, and sexual development in adolescents in
800 relation to environmental pollutants: a feasibility study of biomarkers. Lancet 2001;
801 357:1660-9.

802 Statistics Canada. 2011. Canadian Health Measures Survey (CHMS) Data User Guide:
803 Cycle 1, April 2011. Available at: http://www.statcan.gc.ca/imdb-
804 bmdi/document/5071_D2_T1_V1-eng.pdf%5D. .

805 Toms LM, Calafat AM, Kato K, Thompson J, Harden F, Hobson P, et al. Polyfluoroalkyl
806 chemicals in pooled blood serum from infants, children, and adults in Australia.
807 Environ Sci Technol 2009a; 43:4194-9.

808 Toms LM, Sjodin A, Harden F, Hobson P, Jones R, Edenfield E, et al. Serum
809 polybrominated diphenyl ether (PBDE) levels are higher in children (2-5 years of
810 age) than in infants and adults. Environ Health Perspect 2009b; 117:1461-5.

811 Verner MA, Ayotte P, Muckle G, Charbonneau M, Haddad S. A physiologically based
812 pharmacokinetic model for the assessment of infant exposure to persistent organic
813 pollutants in epidemiologic studies. Environ Health Perspect 2009; 117:481-7.

814 Verner MA, Sonneborn D, Lancz K, Muckle G, Ayotte P, Dewailly E, et al.
815 Toxicokinetic modeling of persistent organic pollutant levels in blood from birth to
816 45 months of age in longitudinal birth cohort studies. Environ Health Perspect 2013;
817 121:131-7.

818

819 Table 1: Sample sizes and actual age ranges sampled for studies included in analysis.

820

Study (Years of Survey, analytes)	N by Nominal Age Group (Actual age range, if different)					
	0-4	5-15	16-30	31-45	46-60	61+
GerES III (1998, PCBs, OCPs)	-	-	621 (18-30)	1013	841	349 (61-69)
GerES IV (2003-2006, PCBs, OCPs)	-	1062 (7-14)	-	-	-	-
NHANES (2003-2004, subsample b, OCPs, PBDEs)	-	298 (12-15)	571	364	285	443 (61-85)
NHANES (2003-2004, subsample c, PCBs)	-	256 (12-15)	598	351	231	435 (61-85)
NHANES (1999-2000, PFCs)	-	278 (12-15)	486	281	193	353 (61-85)
NHANES (2009-2010, subsample c, PFCs)	-	179 (12-15)	526	465	486	577 (61-80)
CHMS (2007-2009, all analytes)	-	-	436 (20-30)	907	695	841 (61-79)
CHIS (2001-2002, PCBs, OCPs)	-	-	186 (18-30)	287	274	172 (61-74)
FLEHS II (PCBs, OCPs)	250 (newborn)	555 (13-15)	46	-	-	-
FLEHS II (PBDE 47)		555 (13-15)	47	-	-	-
FLEHS II (PFCs)	220 (newborn)	168 (13-15)	84	146 (31-40)	-	-

821

822

823

824 Table 2: Unified P95:mean ratios based on NHANES, GerES, and CHIS datasets by age group and overall for PCBs 138, 153, and

825 180; HCB; and DDE.

	Unified P95:mean ratio (95% CI)				
Age Group	PCB 138	PCB 153	PCB 180	HCB	DDE
5-15	2.40 (2.09-2.67)	2.51 (2.05-3.77)	2.91 (2.19-5.44)	1.87 (1.62-2.46)	3.11 (2.4-4.72)
16-30	2.25 (1.99-2.73)	2.23 (1.86-2.86)	2.40 (1.78-3.04)	2.23 (1.63-2.93)	2.56 (1.97-3.66)
31-45	2.06 (1.81-2.57)	2.06 (1.89-2.45)	2.09 (1.87-3.44)	2.51 (1.53-3.04)	2.69 (2.14-3.55)
46-60	2.08 (1.74-2.93)	2.14 (1.92-2.78)	2.00 (1.72-2.49)	2.43 (1.44-2.91)	3.16 (2.63-3.86)
61+	2.14 (1.64-3.12)	2.23 (1.73-3.01)	2.05 (1.71-2.98)	2.41 (1.62-3.27)	3.11 (2.51-3.83)
All ages	2.20 (1.80-3.00)	2.18 (1.83-2.92)	2.12 (1.76-3.36)	2.29 (1.49-3.02)	2.96 (2.12-3.91)

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827

828

829 Table 3: Ratios applied to FLEHS II arithmetic mean concentrations and Australian pool concentrations to estimate 95th

830 percentiles.

Analyte	P95:mean Ratio (95% CI) by Age Group Source					
	0-4	5-15	16-30	31-45	46-60	61+
PCB 138	2.2 (1.8-3) Unified All-Ages (Table 2)					
PCB 153	2.18 (1.8-2.9) Unified All-Ages (Table 2)					
PCB 180	2.12 (1.8-3.4) Unified All-Ages (Table 2)					
HCB	2.3 (1.5-3.0) Unified All-Ages (Table 2)					
DDE	3.0 (2.1-3.9) Unified All-Ages (Table 2)					
PBDE 47	3.3 (2.3-4.1) NHANES 2003-2004 Ages 12-15	3.3 (2.3-4.1) NHANES 2003-2004 Ages 12-15	3.2 (2.5-4.2) NHANES 2003-2004 Age-specific	2.7 (1.9-3.5) NHANES 2003-2004 Age-specific	4.8 (3.4-7) NHANES 2003-2004 Age-specific	4.2 (3.3-5) NHANES 2003-2004 Ages 61-80
PFOA	1.8 (1.6-2.0) NHANES 2009-2010 Ages 12-15	1.8 (1.6-2.0) NHANES 2009-2010 Ages 12-15	2.0 (1.9-2.3) NHANES 2009-2010 Age-specific	2.2 (2.0-2.5) NHANES 2009-2010 Age-specific	2 (1.7-2.5) NHANES 2009-2010 Age-specific	2 (1.9-2.3) NHANES 2009-2010 Ages 61-80
PFOS	2.3 (1.9-3.1) NHANES 2009-2010 Ages 12-15	2.3 (1.9-3.1) NHANES 2009-2010 Ages 12-15	2.1 (1.9-2.5) NHANES 2009-2010 Age-specific	2.6 (2.2-2.6) NHANES 2009-2010 Age-specific	2.3 (2-3.2) NHANES 2009-2010 Age-specific	2.5 (2.3-2.8) NHANES 2009-2010 Ages 61-80

831 Table 4: Arithmetic means (95% CIs) of pooled sample concentrations (4 pools of 100
832 samples per age group) from the Australian 2011-2012 sampling campaign and estimated
833 95th percentiles with 95% CIs for the target analytes.

Compound	Age Group	2011-2012 Mean (95%CI)	Estimated 95th %ile (95%CI)
PCB 138	0-4	3 (1.3-4.6)	6.5 (5.3-8.9)
(ng/g lipid)	5-15	2.1 (0.5-3.6)	4.6 (3.7-6.2)
	16-30	2.2 (1.5-3)	4.9 (4-6.7)
	31-45	3.4 (2.7-4)	7.4 (6-10.1)
	46-60	7.1 (5.2-9)	15.6 (12.8-21.3)
	61+	13.4 (11-15.7)	29.4 (24-40.1)
PCB 153	0-4	3.8 (1.6-5.9)	8.2 (6.9-11)
(ng/g lipid)	5-15	2.9 (0.2-5.7)	6.4 (5.4-8.5)
	16-30	2.8 (1.7-3.9)	6.2 (5.2-8.2)
	31-45	4.7 (3.5-5.9)	10.2 (8.6-13.7)
	46-60	10.1 (7.7-12.5)	22.1 (18.5-29.6)
	61+	18.9 (16.9-20.9)	41.3 (34.6-55.3)
PCB 180	0-4	2.5 (0.9-4.1)	5.3 (4.4-8.4)
(ng/g lipid)	5-15	2.3 (0.4-4.1)	4.8 (4-7.6)
	16-30	2.4 (1.3-3.5)	5 (4.2-8)
	31-45	4.2 (2.9-5.5)	9 (7.4-14.2)
	46-60	9.7 (6.7-12.7)	20.6 (17.1-32.6)
	61+	18.5 (15.3-21.6)	39.2 (32.5-62.1)
HCB	0-4	5 (3.7-6.2)	11.3 (7.4-14.9)
(ng/g lipid)	5-15	3.4 (2.3-4.5)	7.8 (5.1-10.3)
	16-30	3.6 (2.6-4.5)	8.1 (5.3-10.7)
	31-45	4.4 (3.1-5.8)	10.1 (6.6-13.4)
	46-60	9.9 (3.4-16.3)	22.6 (14.7-29.7)
	61+	36.4 (0-85)	83.3 (54.2-109.9)
DDE	0-4	145 (23.9-266)	429.1 (307.3-566.8)
(ng/g lipid)	5-15	82.7 (24.7-140.7)	244.7 (175.3-323.3)
	16-30	104.9 (3.4-206.4)	310.5 (222.4-410.2)
	31-45	115 (95-135)	340.3 (243.7-449.6)
	46-60	277.5 (208.2-346.7)	821.3 (588.2-1084.9)
	61+	664.9 (298.6-1031.2)	1968 (1409.5-2599.7)
PBDE 47	0-4	6.3 (4.9-7.8)	21.1 (14.6-25.7)
(ng/g lipid)	5-15	5.8 (3.6-7.9)	19.2 (13.3-23.3)
	16-30	3.8 (2.8-4.7)	12 (9.5-15.8)
	31-45	3.4 (2.5-4.3)	9.1 (6.5-11.8)
	46-60	2.8 (1.6-4)	13.3 (9.3-19.3)
	61+	3.3 (0.9-5.6)	13.6 (10.7-16.3)
PFOA	0-4	5.2 (3.2-7.1)	9.2 (8.3-10.1)
(ng/ml)	5-15	4.5 (3.7-5.3)	8 (7.2-8.8)
	16-30	4.2 (3.1-5.3)	8.6 (8-9.5)
	31-45	3.7 (2.7-4.6)	8.1 (7.2-9.3)
	46-60	4.2 (3.1-5.4)	8.4 (7.3-10.4)
	61+	5 (4.2-5.9)	10 (9.3-11.6)
PFOS	0-4	5.7 (3.5-7.8)	13.2 (10.9-17.5)
(ng/ml)	5-15	8 (5.8-10.2)	18.8 (15.5-24.9)
	16-30	9.8 (6.4-13.1)	20.3 (18.5-24.1)
	31-45	10 (4.5-15.5)	25.5 (22.3-29.4)
	46-60	12.9 (6.8-19)	29.7 (26.3-40.8)
	61+	15.1 (10.4-19.9)	37.8 (34.6-41.6)

834

835 Table 5: Available health risk-based screening criteria for target analytes based on non-

836 cancer toxicity endpoints (reviewed in Aylward et al. 2013).

	Exposure Guidance Value	External Dose value	Toxicity Endpoint	BE or Biomarker Guidance Value (ng/g lipid)
HCB	MRL, ATSDR, 2002	5E-05 mg/kg-d	Hepatic toxicity in rats	47 ng/g lipid
DDE	EPA RfD, 1996	5E-04 mg/kg-d (as DDT)	Hepatic toxicity in rats	5000 ng/g lipid[1]
PCBs	ANSES "concentration of concern", 2010	NA	Neurodevelopmental endpoints in infants and children; various endpoints in other adults	700 ng/g[2] lipid (infants, children, women of chlidbearing age) 1800 ng/g lipid (other adults)

837 NA, not applicable. BE, biomonitoring equivalents.
838 [1] As sum of DDT, DDE, DDD
839 [2] Sum of PCBs 138, 153, and 180 x 1.7.
840
841

842 Figure captions

843 Figure 1: PCBs 138, 153, and 180. The panel on the left shows the arithmetic means for
844 each included population with the 95% confidence interval on the mean. The panel on the
845 right shows the P95:mean ratio with 95% CI based on bootstrapping as described in the
846 text.

847

848 Figure 2: HCB, DDE, and PBDE 47. See Figure 1 legend for description of the figures.

849

850 Figure 3: PFOA and PFOS. See Figure 1 legend for description of the figures.

851

852 Figure 4: Arithmetic means (bars) and observed 95th percentiles (squares) from the FLEHS
853 II dataset, and predicted 95th percentiles (triangles) based on application of the P95:mean
854 ratios identified in Table 3 to the arithmetic mean concentrations in the FLEHS II dataset.

855

856

857

Supplementary Data

Population Variation in Biomonitoring Data for Persistent Organic Pollutants (POPs): An Examination of Multiple Population-Based Datasets for Application to Australian Pooled Biomonitoring Data

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Summary Statistical Tables for Included Surveys

This project examined available biomonitoring datasets from the US National Health and Nutrition Examination Survey (NHANES), the Canadian Health Measures Survey (CHMS), the German Environmental Survey (GerES), the Catalan Health Interview Survey (CHIS), and the Flemish Environmental Health Survey II (FLEHS II) to inform interpretation of the Australian pooled biomonitoring data. Tables of summary statistics for the GerES (Table

884 S1), the CHIS (Table S2), NHANES (Table S3), CHMS (Table S4), and FLEHS II (Table S5) are
885 presented here.

886

887 Table S1: Arithmetic mean (AM), geometric mean (GM), geometric standard deviation
888 (GSD), 95th percentile (p95), and P95:AM ratios from the German Environmental Survey
889 (GerES). Note that for age group 7-14 data are from GerES IV, from samples collected from
890 2003-2006, while the data for the remaining age groups was from the GerES III, conducted
891 in 1998. Concentrations measured in whole blood.

892

Compound	Age Group	AM (95%CI)	GM	GSD	p95	P95:AM ratio (95% CI)
PCB 138	7-14	0.11 (0.11, 0.12)	0.09	2.08	0.27	2.4 (2.27, 2.61)
(ug/L)	16-30	0.24 (0.22, 0.25)	0.19	1.90	0.53	2.3 (2.01, 2.45)
	31-45	0.46 (0.43, 0.48)	0.38	1.85	0.93	2.0 (1.96, 2.19)
	46-60	0.74 (0.71, 0.77)	0.63	1.78	1.50	2.0 (1.95, 2.15)
	61+	0.96 (0.89, 1.03)	0.82	1.73	1.98	2.0 (1.88, 2.21)
PCB 153	7-14	0.17 (0.16, 0.18)	0.13	2.06	0.43	2.6 (2.35, 2.82)
(ug/L)	16-30	0.37 (0.35, 0.39)	0.31	1.90	0.86	2.3 (2.08, 2.48)
	31-45	0.73 (0.7, 0.77)	0.61	1.88	1.46	2.0 (1.9, 2.12)
	46-60	1.19 (1.15, 1.24)	1.03	1.77	2.38	2.0 (1.93, 2.08)
	61+	1.51 (1.41, 1.63)	1.32	1.69	3.11	2.1 (1.82, 2.39)
PCB 180	7-14	0.1 (0.09, 0.1)	0.07	2.49	0.28	2.9 (2.71, 3.11)
(ug/L)	16-30	0.21 (0.2, 0.23)	0.16	2.11	0.50	2.4 (2.25, 2.69)
	31-45	0.49 (0.47, 0.52)	0.40	1.90	1.02	2.1 (1.95, 2.17)
	46-60	0.85 (0.82, 0.88)	0.72	1.83	1.71	2.0 (1.92, 2.12)
	61+	1.07 (0.99, 1.15)	0.91	1.73	2.09	2.0 (1.7, 2.21)
DDE	7-14	0.3 (0.28, 0.33)	0.21	2.28	0.91	3.0 (2.78, 3.54)
(ug/L)	16-30	1.04 (0.96, 1.13)	0.76	2.15	2.72	2.6 (2.36, 2.97)
	31-45	2.16 (2.02, 2.32)	1.43	2.41	6.73	3.1 (2.8, 3.63)
	46-60	3.52 (3.25, 3.8)	2.29	2.58	11.18	3.2 (2.84, 3.47)
	61+	4.42 (3.94, 4.94)	3.10	2.31	13.37	3.0 (2.71, 3.29)
HCB	7-14	0.11 (0.11, 0.11)	0.10	1.61	0.20	1.9 (1.77, 2.03)
(ug/L)	16-30	0.21 (0.19, 0.24)	0.16	2.01	0.47	2.2 (2.05, 2.47)
	31-45	0.49 (0.46, 0.54)	0.34	2.31	1.31	2.7 (2.43, 3.19)
	46-60	1.05 (0.99, 1.12)	0.76	2.35	2.66	2.5 (2.3, 2.74)
	61+	1.89 (1.61, 2.25)	1.22	2.48	5.23	2.8 (2.37, 3.47)

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Table S2: Arithmetic mean (AM), geometric mean (GM), geometric standard deviation (GSD), 95th percentile (p95), and P95:AM ratios from the Catalan Health Interview Survey (CHIS).

Compound	Age Group	AM (95%CI)	GM	GSD	p95	P95:AM ratio (95% CI)
PCB 138	16-30	45.3 (40.2, 51.1)	33.1	2.5	101.3	2.2 (1.9, 3)
(ng/g lipid)	31-45	74.2 (65.9, 84.9)	56.1	2.4	145.0	2.0 (1.8, 2.5)
	46-60	118.7 (99, 149.6)	90.7	2.1	235.4	2.0 (1.7, 2.4)
	60+	145.2 (127.4, 165.3)	121.5	1.8	284.9	2.0 (1.5, 2.8)
PCB 153	16-30	60.6 (54.5, 67.2)	47.2	2.3	122.5	2.0 (1.8, 2.6)
(ng/g lipid)	31-45	99.7 (92.5, 108.4)	84.2	2.0	209.4	2.1 (1.8, 2.3)
	46-60	149.5 (136.5, 162.2)	124.4	2.1	329.7	2.2 (1.9, 2.5)
	60+	209.2 (183, 238.8)	171.9	1.9	528.5	2.5 (1.7, 2.9)
PCB 180	16-30	48.9 (44.7, 54)	40.7	1.9	98.7	2 (1.7, 2.4)
(ng/g lipid)	31-45	83.1 (77.3, 89.5)	74.3	1.6	171.9	2.1 (1.8, 2.2)
	46-60	114.5 (104.2, 125.5)	99.0	1.7	228.9	2 (1.7, 2.2)
	60+	149.8 (131.3, 171.1)	124.4	1.7	341.3	2.3 (1.7, 3.2)
DDE	16-30	262.9 (219.1, 313.8)	196.1	2.0	548.5	2.1 (1.9, 4)
(ng/g lipid)	31-45	515.8 (450, 595.1)	373.7	2.2	1185.4	2.3 (2.1, 3)
	46-60	995.5 (851.5, 1148.5)	648.7	2.6	3532.4	3.5 (2.5, 4.1)
	60+	1267.4 (1079, 1478.7)	878.6	2.5	3910.8	3.1 (2.4, 3.6)
HCB	16-30	88.1 (73, 106.3)	54.7	3.0	240.2	2.7 (2.2, 3.1)
(ng/g lipid)	31-45	184.4 (162, 211.2)	106.0	3.8	472.0	2.6 (2.3, 3.1)
	46-60	375.8 (329, 423.9)	254.5	2.7	971.9	2.6 (2.2, 3)
	60+	532 (455, 610.2)	383.7	2.4	1302.7	2.4 (2.1, 2.8)

Table S3: Arithmetic mean (AM), geometric mean (GM), geometric standard deviation (GSD), 95th percentile (p95), and P95:AM ratios from the US National Health and Nutrition Examination Survey (NHANES) datasets. Summary statistics for two cycles of collection for PFOA and PFOS are presented: 1999-2000, and 2009-2010.

Compound	Age Group	AM (95%CI)	GM	GSD	p95	P95:AM ratio (95% CI)
PCB 138	12-15	5.8 (4.6, 7)	4.6	1.9	14.5	2.5 (2, 2.8)
(ng/g lipid)	16-30	7.9 (7.1, 8.8)	6.4	1.9	18.8	2.4 (2.1, 2.8)
	31-45	18.1 (15.7, 20.4)	14.2	2.0	38.5	2.1 (2, 2.8)
	46-60	31.8 (25, 38.5)	25.2	2.0	75.8	2.4 (2.1, 3.1)
	60+	52.4 (45.7, 59.2)	41.1	2.0	135.0	2.6 (2.4, 3.2)
PCB 153	12-15	7.4 (5.8, 8.9)	5.4	2.0	18.5	2.5 (2, 4)
(ng/g lipid)	16-30	10.1 (8.9, 11.3)	7.9	2.0	21.9	2.2 (2, 2.9)
	31-45	23.2 (20, 26.4)	18.5	2.0	49.8	2.1 (2, 2.5)
	46-60	42.7 (35, 50.5)	34.7	1.9	103.0	2.4 (2.1, 2.9)
	60+	68.8 (60.8, 76.8)	56.8	1.8	169.0	2.5 (2.2, 3.1)
PCB 180	12-15	4.9 (3.7, 6.2)	2.8	2.7	14.8	3 (2, 5.8)
(ng/g lipid)	16-30	6.7 (5.9, 7.5)	4.8	2.3	18.5	2.8 (2.4, 3.5)
	31-45	19.5 (16.1, 22.8)	15.3	2.0	44.6	2.3 (2, 3.5)
	46-60	36 (31.8, 40.3)	30.9	1.8	75.8	2.1 (1.8, 2.6)
	60+	57.9 (50.6, 65.1)	50.2	1.7	117.0	2 (1.9, 2.3)
DDE	12-15	195.5 (123.5, 267.5)	98.1	2.7	637.0	3.3 (2.3, 5.4)
(ng/g lipid)	16-30	220.1 (159, 281.1)	125.5	2.4	577.0	2.6 (2, 3.2)
	31-45	409.2 (288.9, 529.5)	211.5	2.6	1020.0	2.5 (2.1, 3.2)
	46-60	602 (415.5, 788.5)	341.3	2.8	1870.0	3.1 (2.7, 3.7)
	60+	1090.9 (845.2, 1336.7)	591.6	3.2	3970.0	3.6 (2.7, 4)
HCB	12-15	14.6 (13.4, 15.7)	13.1	1.6	27.4	1.9 (1.6, 2.6)
(ng/g lipid)	16-30	14.3 (13.2, 15.3)	13.2	1.4	24.4	1.7 (1.6, 1.8)
	31-45	16.4 (14.6, 18.2)	14.7	1.5	26.5	1.6 (1.5, 1.8)
	46-60	17.5 (16, 19)	15.9	1.5	26.4	1.5 (1.4, 1.7)
	60+	20.8 (19.5, 22.1)	19.2	1.5	37.4	1.8 (1.6, 2)
PBDE 47	12-15	43.2 (35.2, 51.1)	28.6	2.5	144.0	3.3 (2.3, 4.1)
(ng/g lipid)	16-30	45.7 (33.9, 57.6)	24.3	2.8	146.0	3.2 (2.5, 4.2)
	31-45	40.3 (23.3, 57.3)	18.8	2.9	109.0	2.7 (1.9, 3.5)
	46-60	50 (31.7, 68.3)	18.5	3.7	240.0	4.8 (3.4, 7)
	60+	51.1 (33.7, 68.5)	18.9	3.8	214.0	4.2 (3.3, 5)
PFOA (09-10)	12-15	3 (2.5, 3.4)	2.7	1.6	5.3	3 (2.5, 3.4)
(ng/ml)	16-30	3.4 (3, 3.8)	2.9	1.9	7.0	3.4 (3, 3.8)
	31-45	3.3 (2.9, 3.7)	2.8	1.9	7.4	3.3 (2.9, 3.7)
	46-60	3.8 (3.4, 4.2)	3.3	1.8	7.6	3.8 (3.4, 4.2)
	60+	4.2 (3.6, 4.8)	3.5	1.9	8.4	4.2 (3.6, 4.8)
PFOS (09, 10)	12-15	7.7 (5.8, 9.7)	6.4	1.8	18.1	2.3 (1.9, 3.1)
(ng/ml)	16-30	9.6 (8, 11.2)	7.6	2.0	20.0	2.1 (1.9, 2.5)
	31-45	10.5 (7.9, 13.2)	7.7	2.2	26.9	2.6 (2.2, 3)
	46-60	14 (11.1, 16.9)	10.7	2.0	32.2	2.3 (2, 3.2)
	60+	18.5 (14.5, 22.5)	13.5	2.2	46.2	2.5 (2.3, 2.8)
PFOA (99, 00)	12-15	6.4 (5.6, 7.1)	5.8	1.6	11.9	1.9 (1.7, 2.7)
(ng/ml)	16-30	5.8 (5.3, 6.4)	5.2	1.6	11.0	1.9 (1.7, 2.2)
	31-45	6.4 (4.9, 7.9)	5.3	1.7	11.1	1.7 (1.5, 2.2)
	46-60	6.7 (5.3, 8.1)	5.4	1.8	14.6	2.2 (1.7, 2.6)
	60+	5.8 (4.4, 7.3)	4.8	1.9	11.5	2 (1.7, 2.4)
PFOS (99, 00)	12-15	34.3 (30.2, 38.3)	31.3	1.6	57.6	1.7 (1.6, 1.9)
(ng/ml)	16-30	31.1 (27.8, 34.5)	27.7	1.6	56.8	1.8 (1.7, 2.2)
	31-45	36.2 (28.9, 43.6)	29.5	1.8	76.5	2.1 (1.8, 2.8)
	46-60	38.8 (32.3, 45.3)	33.2	1.8	78.3	2 (1.8, 2.6)
	60+	40 (33.5, 46.5)	33.5	1.9	97.5	2.4 (1.9, 2.8)

905 Table S4: Arithmetic mean (AM), 95th percentile (p95), and P95:AM ratios from the
906 Canadian Health Measures Survey (CHMS). Geometric means and geometric standard
907 deviations were not available for this tabulation.

Compound	Age Group	AM (95%CI)	P95	P95:AM ratio (95% CI)
PCB 138	16-30	6.1 (4.7, 7.4)	14	2.3 (2, 3.8)
(ng/g lipid)	31-45	9.5 (8.2, 11)	24	2.5 (2.2, 2.7)
	46-60	19 (16, 22)	48	2.6 (2.3, 3.3)
	60+	28 (24, 33)	68	2.4 (2.1, 2.8)
PCB 153	16-30	10 (7.4, 14)	28	2.7 (1.9, 3.8)
(ng/g lipid)	31-45	17 (14, 20)	39	2.3 (2, 2.7)
	46-60	36 (29, 43)	96	2.6 (2.3, 3.5)
	60+	55 (48, 63)	140	2.5 (2, 2.8)
PCB 180	16-30	7.7 (4.5, 11)	--[a]	2.3 (1.7, 4.2)
(ng/g lipid)	31-45	14 (11, 16)	30	2.2 (2, 2.6)
	46-60	33 (25, 41)	--[a]	2.3 (2, 4.5)
	60+	53 (46, 60)	140	2.6 (2, 3)
DDE	16-30	150 (110, 200)	--[a]	3.2 (2.7, 5.8)
(ng/g lipid)	31-45	250 (140, 350)	--[a]	3.6 (2.1, 6)
	46-60	310 (200, 420)	1000	3.2 (2.6, 4.3)
	60+	680 (280, 1100)	1600	2.4 (1.9, 3.8)
HCB	16-30	8.1 (7.1, 9.1)	16	2 (1.8, 2.3)
(ng/g lipid)	31-45	12 (9.5, 15)	33	2.7 (1.8, 3.4)
	46-60	13 (10, 16)	26	2 (1.7, 2.3)
	60+	17 (14, 21)	35	2 (1.6, 2.7)
PBDE 47	16-30	26 (18, 34)	100	3.8 (2.7, 5.8)
(ng/g lipid)	31-45	16 (13, 20)	62	3.8 (2.9, 4.1)
	46-60	23 (14, 32)	62	2.7 (2.1, 3.5)
	60+	24 (17, 31)	71	3 (2.5, 3.8)
PFOA	16-30	2.9 (2.7, 3.1)	5.4	1.9 (1.7, 2)
(ng/ml)	31-45	2.7 (2.5, 2.9)	5.1	1.9 (1.8, 2)
	46-60	2.9 (2.7, 3.1)	5.5	1.9 (1.8, 2)
	60+	3.2 (3, 3.4)	6.2	2 (1.8, 2.1)
PFOS	16-30	10 (9, 11)	20	1.9 (1.8, 2.6)
(ng/ml)	31-45	11 (8.8, 13)	24	2.2 (1.9, 3.1)
	46-60	11 (9.8, 12)	29	2.6 (2.2, 2.9)
	60+	14 (12, 15)	30	2.2 (2-2.4)

908 [a] Estimate not provided due to large coefficient of variation.

909

910 Table S5: Arithmetic mean (AM), geometric mean (GM), geometric standard deviation
911 (GSD), and 95th percentiles (p95) from the Flemish Environment and Health Survey II
912 (FLEHS II). P95:AM ratios were not calculated for this dataset because it was used as a
913 validation dataset.

Compound	Age Group	AM (95% CI)	GM	GSD	p95
PCB 138	Newborn	20.1 (18.6, 21.6)	16.4	2.0	42.3
(ng/g lipid)	13-15	13.3 (12.3, 14.2)	10.7	1.9	29.1
	16-30	14.9 (12, 17.9)	12.2	2.0	39.9
PCB 153	Newborn	31.1 (28.9, 33.3)	26.4	1.8	66.4
(ng/g lipid)	13-15	21.4 (19.9, 22.8)	17.4	1.9	45.6
	16-30	23.3 (19.3, 27.4)	19.9	1.8	58.8
PCB 180	Newborn	18.4 (16.9, 19.9)	14.7	2.0	43.4
(ng/g lipid)	13-15	12.8 (11.7, 14)	9.3	2.2	30.9
	16-30	14 (11.2, 16.8)	11.2	2.0	38.5
HCB	Newborn	12.4 (10.9, 13.9)	9.4	2.0	26.9
(ng/g lipid)	13-15	9.3 (8.8, 9.9)	8	1.7	16.7
	16-30	8.2 (7, 9.3)	7.1	1.8	16
DDE	Newborn	101.3 (90.4, 112.1)	77.7	2.0	270.2
(ng/g lipid)	13-15	84.1 (69.6, 98.5)	54.7	2.2	212.3
	16-30	89 (51, 127.1)	55.4	2.3	484.3
PBDE 47	Newborn	--	--	--	--
(ng/g lipid)	13-15	0.7 (0.6, 0.9)	0.5	2.0	2.2
	16-30	0.6 (0.4, 0.8)	0.4	1.9	3
PFOA	Newborn	1.6 (1.5, 1.7)	1.5	1.5	3
(ug/L)	13-15	2.6 (2.5, 2.8)	2.5	1.3	4
	16-30	3.4 (3.1, 3.7)	3.1	1.6	6.4
	31-45	3.5 (3.3, 3.8)	3.2	1.6	6.3
PFOS	Newborn	3.1 (2.8, 3.3)	2.6	1.7	5.7
(ug/L)	13-15	6.9 (5.8, 7.9)	5.6	1.7	13
	16-30	12.1 (10.1, 14.2)	10	1.8	29.6
	31-45	14.9 (13.4, 16.4)	12.7	1.8	32.4

914

915

Figure(s)

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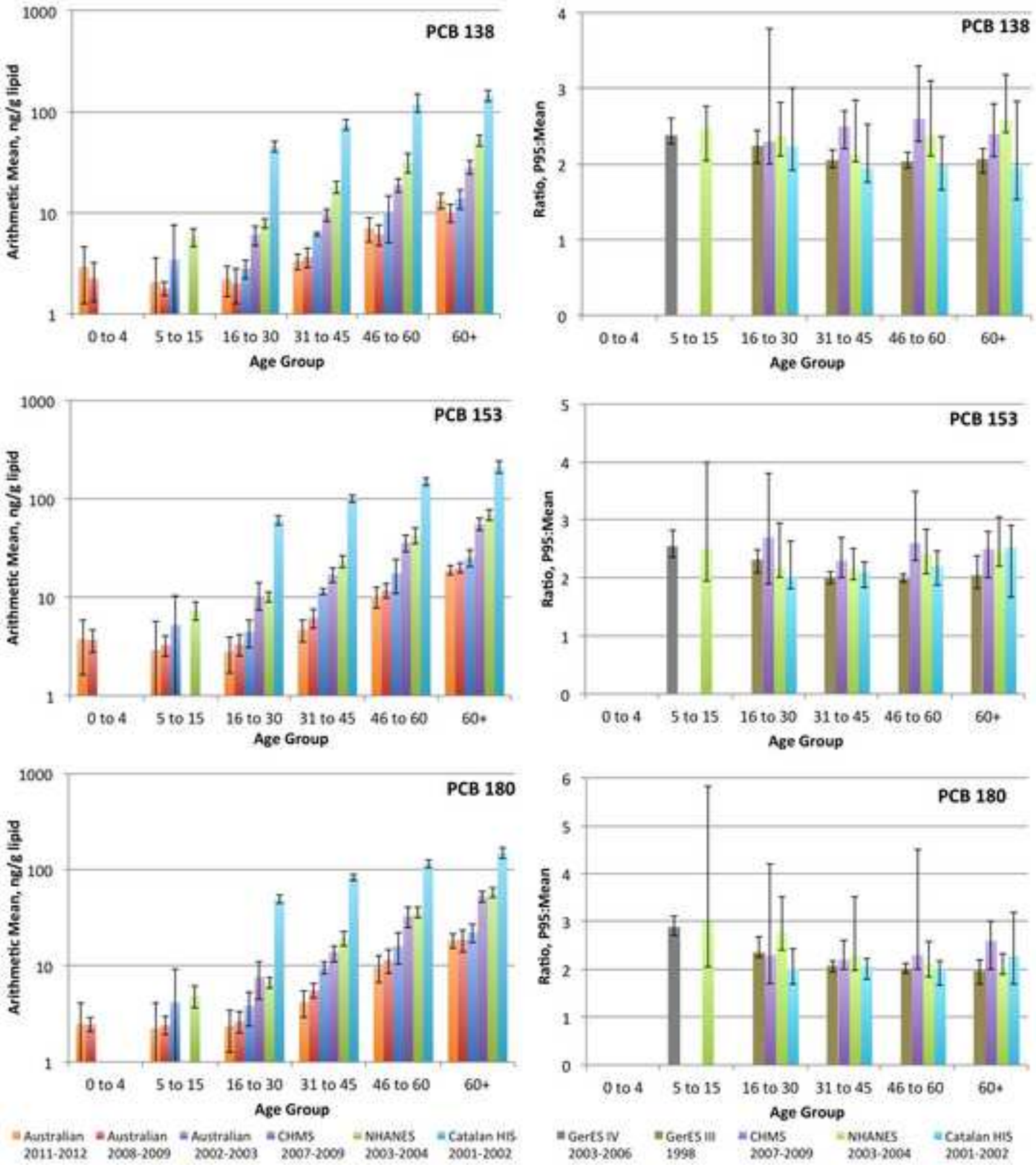

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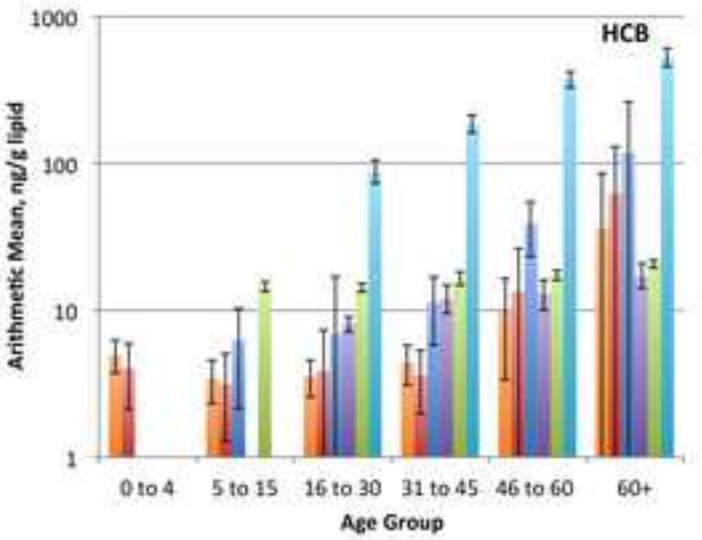

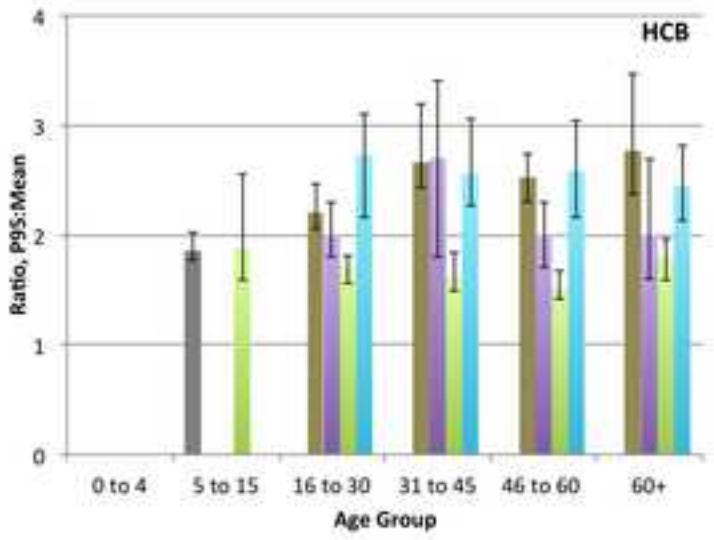

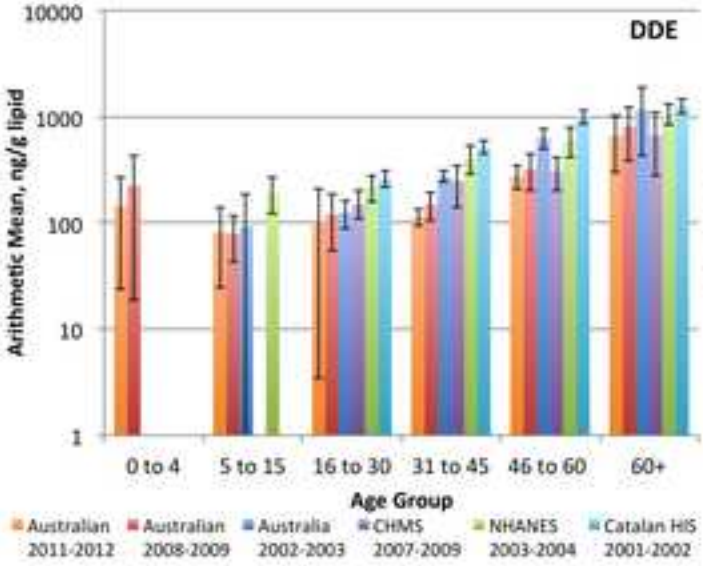

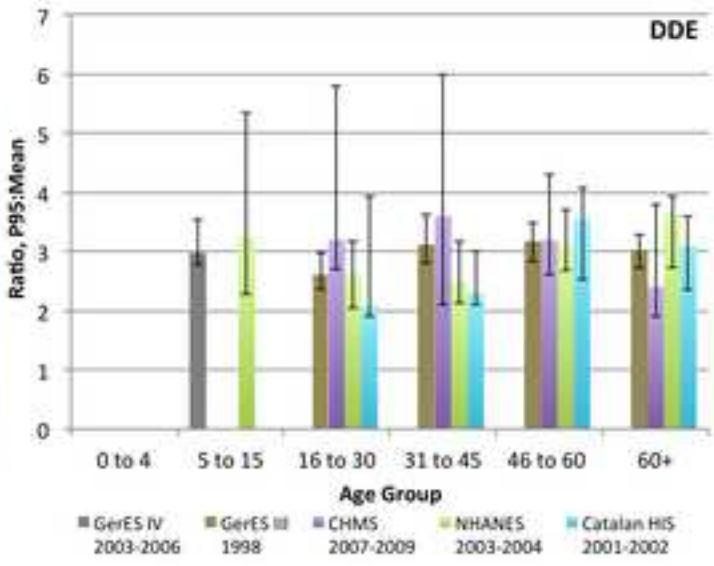

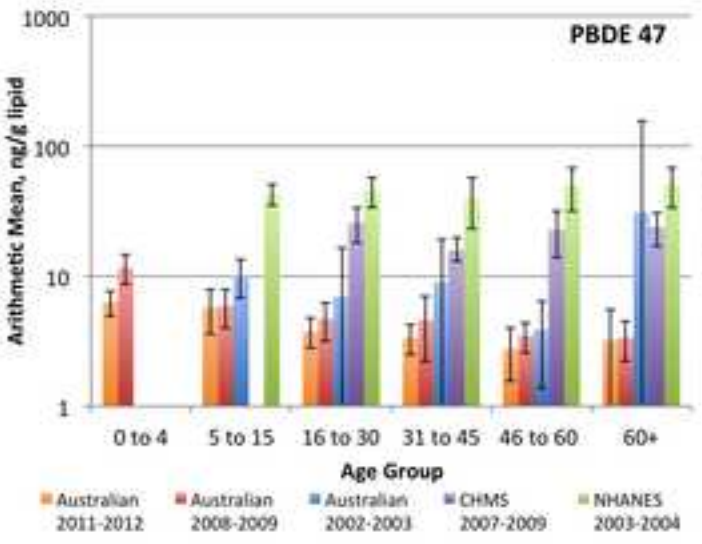

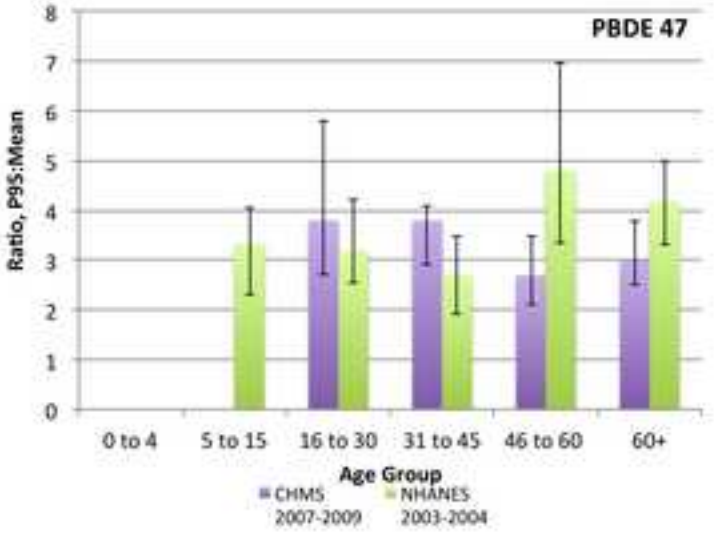

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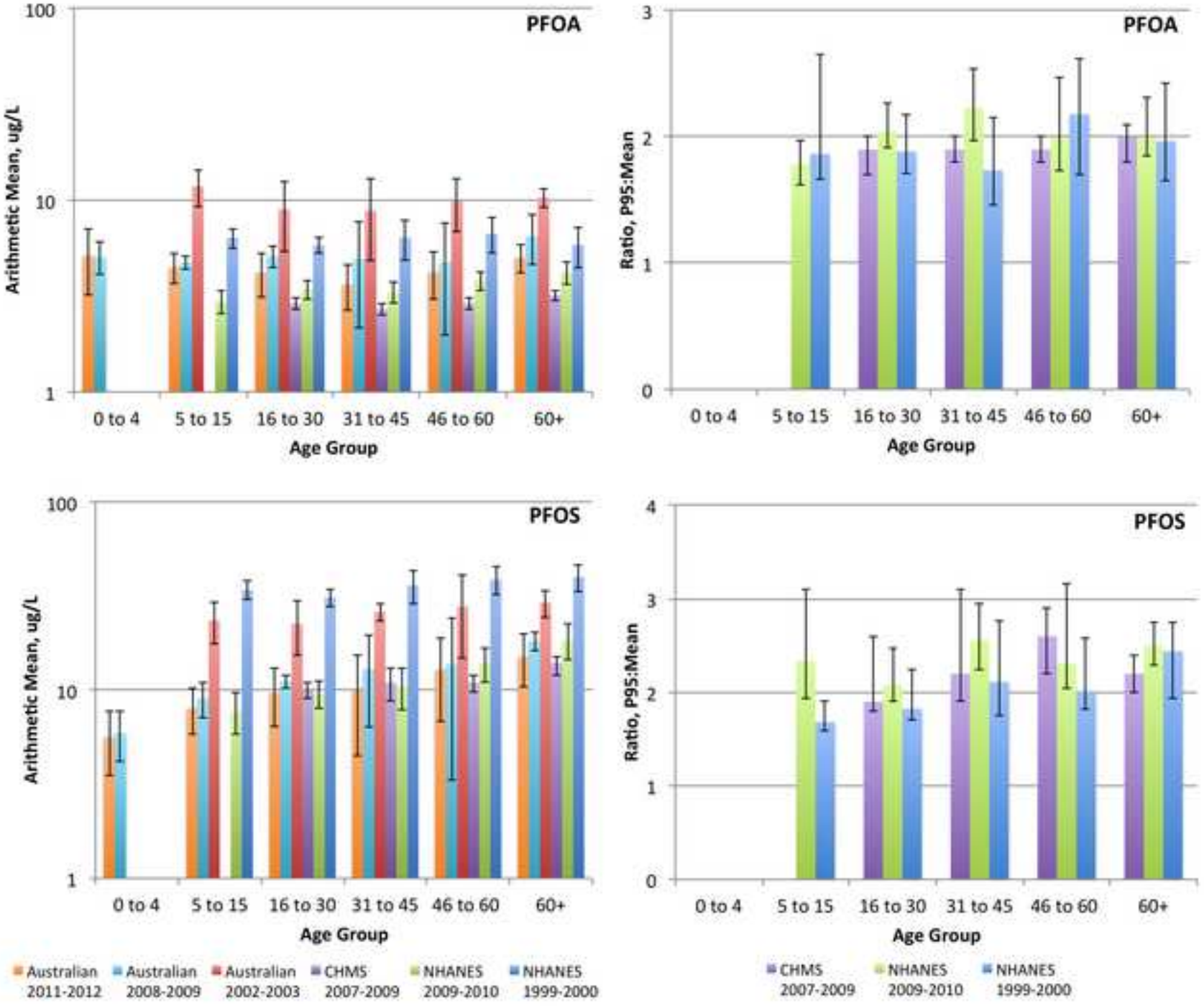

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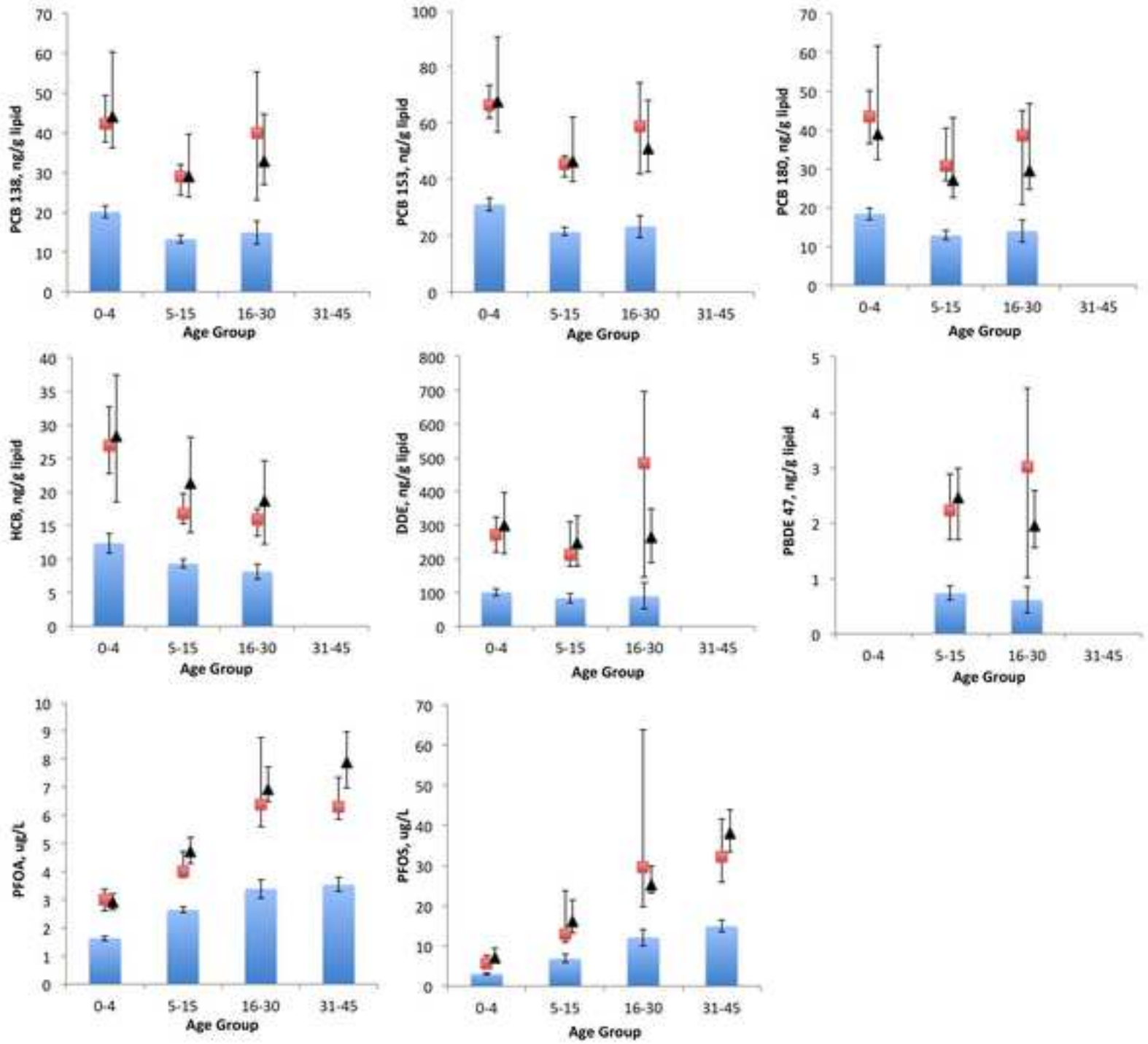

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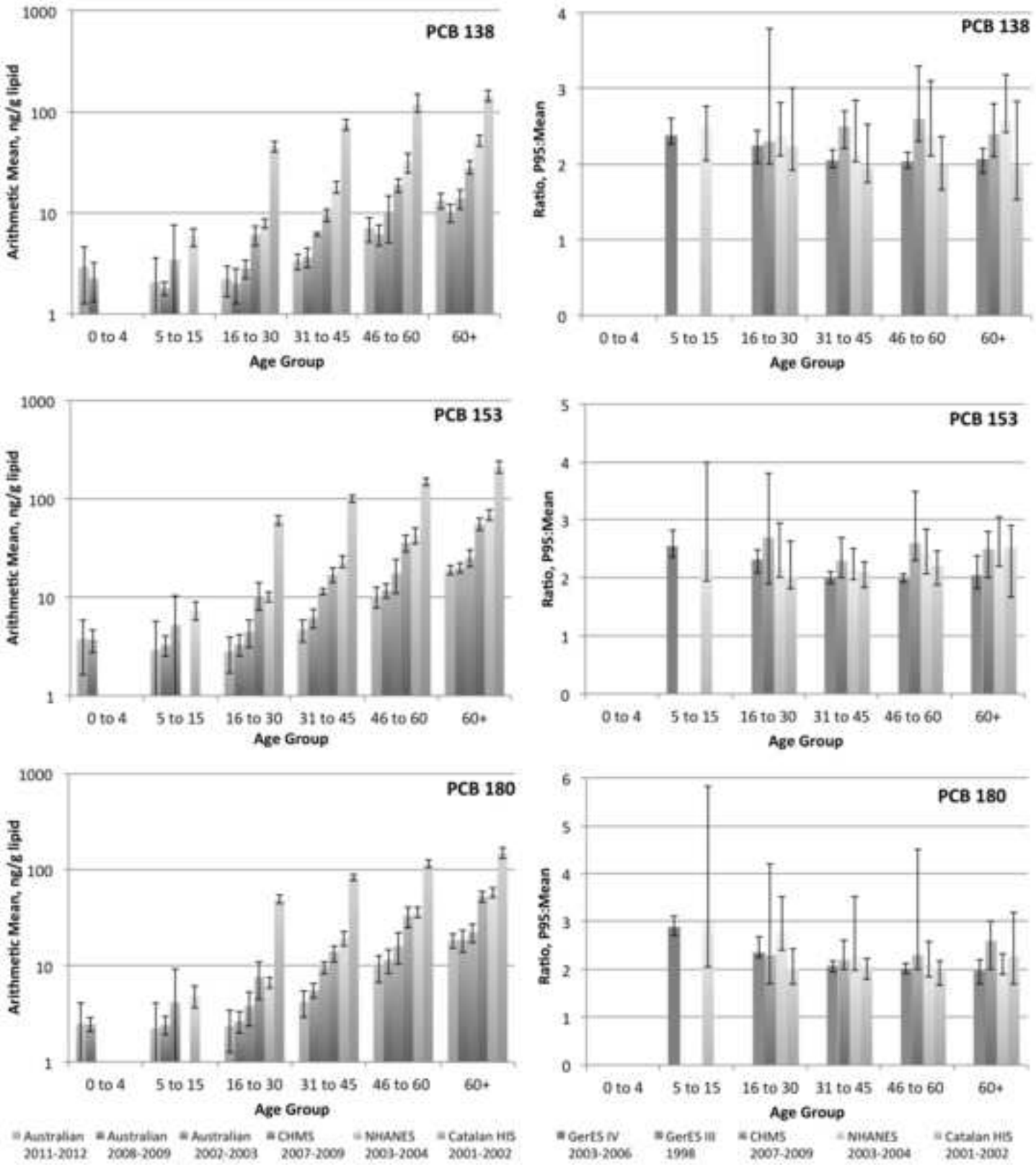

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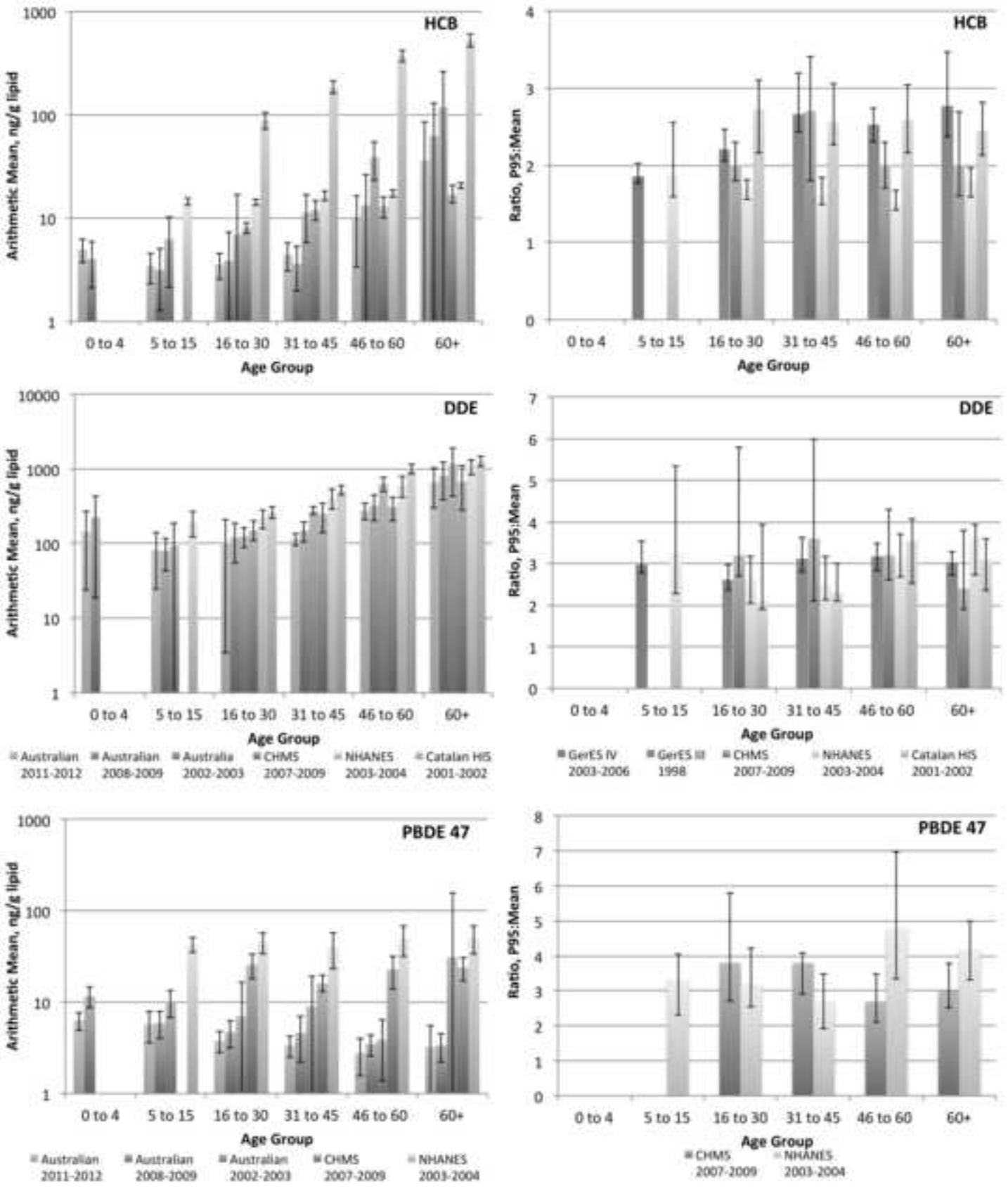

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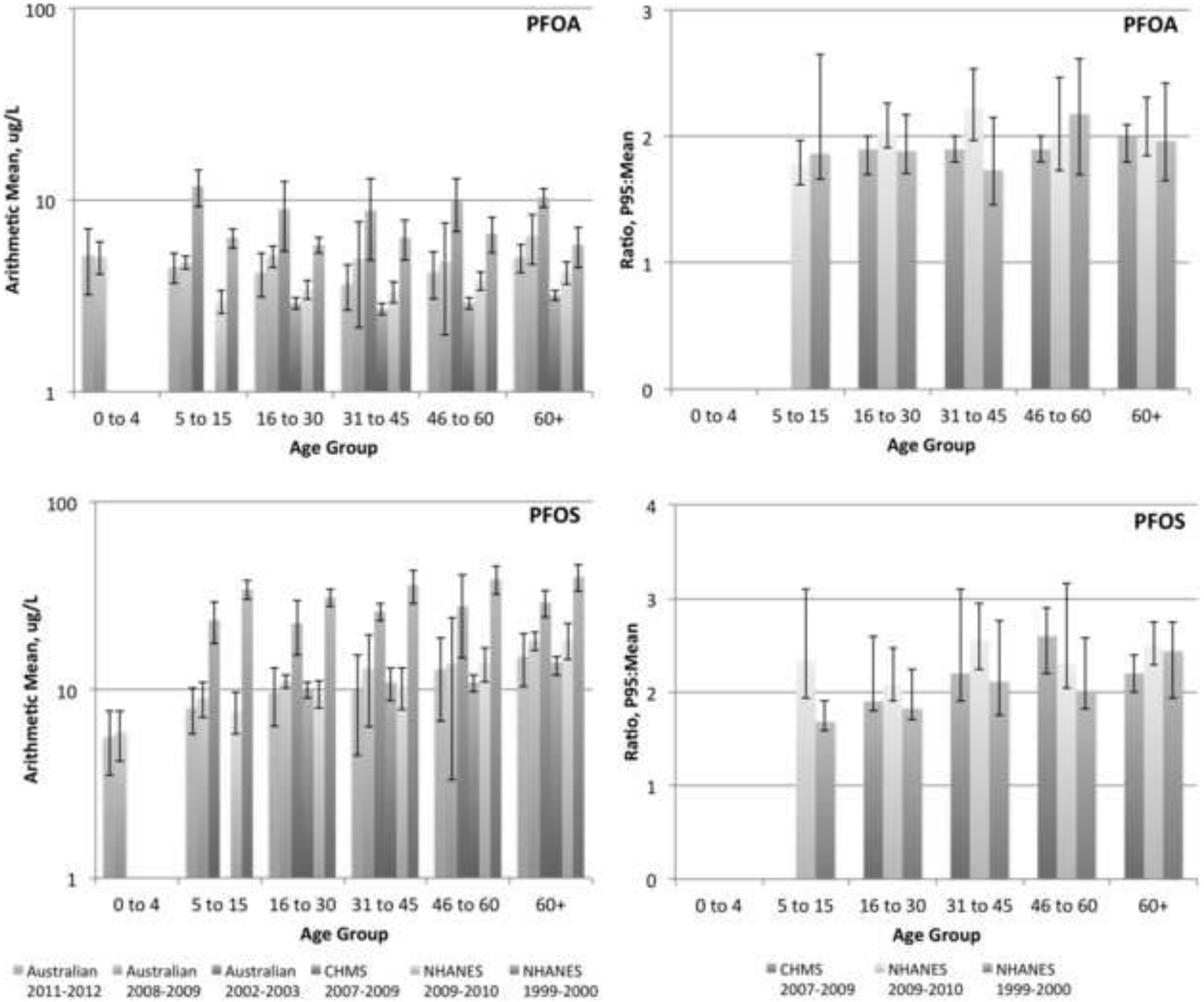

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